

A chromatic feature detector in the retina signals visual context changes

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1 The retina transforms patterns of light into visual feature
2 representations supporting behaviour. These representations
3 are distributed across various types of retinal ganglion cells
4 (RGCs), whose spatial and temporal tuning properties have
5 been studied extensively in many model organisms, including
6 the mouse. However, it has been difficult to link the potentially
7 nonlinear retinal transformations of natural visual inputs to
8 specific ethological purposes. Here, we discover a nonlinear se-
9 lectivity to chromatic contrast in an RGC type that allows the
10 detection of changes in visual context. We trained a convolutional
11 neural network (CNN) model on large-scale functional
12 recordings of RGC responses to natural mouse movies, and then
13 used this model to search *in silico* for stimuli that maxi-
14 mally excite distinct types of RGCs. This procedure predicted
15 centre colour opponency in transient Suppressed-by-Contrast
16 RGCs (tSbC), a cell type whose function is being debated. We
17 confirmed experimentally that these cells indeed responded
18 very selectively to Green-OFF, UV-ON contrasts. This type
19 of chromatic contrast was characteristic of transitions from
20 ground to sky in the visual scene, as might be elicited by head-
21 or eye-movements across the horizon. Because tSbC cells per-
22 formed best among all RGC types at reliably detecting these
23 transitions, we suggest a role for this RGC type in providing
24 contextual information (i.e. sky or ground) necessary for the
25 selection of appropriate behavioural responses to other stimuli,
26 such as looming objects. Our work showcases how a combi-
27 nation of experiments with natural stimuli and computational
28 modelling allows discovering novel types of stimulus selectivity
29 and identifying their potential ethological relevance.

30 retina | colour vision | computational modelling | digital twin | early visual
31 pathway | natural stimuli

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33 Introduction

34 Sensory systems evolved to generate representations of an
35 animal's natural environment useful for survival and pro-
36 creation (1). These environments are complex and high-
37 dimensional, and different features are relevant for different
38 species (reviewed in (2)). As a consequence, the representa-
39 tions are adapted to an animal's needs: features of the world
40 relevant for the animal are represented with enhanced preci-

41 sion, whereas less important features are discarded. Sensory
42 processing is thus best understood within the context of the
43 environment an animal evolved in and that it interacts with
44 (reviewed in (3, 4)).

45 The visual system is well-suited for studying sensory
46 processing, as the first features are already extracted at
47 its experimentally well-accessible front-end, the retina (re-
48 viewed in (2, 7)). In the mouse, this tissue gives rise to
49 around 40 parallel channels that detect different features
50 (6, 8–10), represented by different types of retinal ganglion
51 cells (RGCs), whose axons send information to numerous
52 visual centres in the brain (11). Some of these channels en-
53 code basic features, such as luminance changes and motion,
54 that are only combined in downstream areas to support a
55 range of behaviours such as cricket hunting in mice (12).
56 Other channels directly extract specific features from natu-
57 ral scenes necessary for specific behaviours. For instance,
58 transient OFF- α cells trigger freezing or escape behaviour
59 in response to looming stimuli (13–15).

60 For many RGC types, however, we lack understanding
61 of the features they encode and how these link to behaviour
62 (16). One reason for this is that the synthetic stimuli com-
63 monly used to study retinal processing fail to drive retinal
64 circuits "properly" and, hence, cannot uncover critical re-
65 sponse properties triggered in natural environments. Colour,
66 for example, is a salient feature in nature, and the mouse
67 visual system dedicates intricate circuitry to the processing
68 of chromatic information (17–22). Studies using synthetic
69 stimuli have revealed nonlinear and centre-surround interac-
70 tions between colour channels, but it is not clear how these
71 are engaged in retinal processing of natural environments.

72 Indeed, stimuli capturing the statistics of natural envi-
73 ronments have revealed a larger complexity in retinal spa-
74 tial nonlinearities than had been previously described based
75 on simpler synthetic stimuli (23). Such nonlinearities, cru-
76 cial for the encoding of natural stimuli, cannot be captured
77 by Linear-Nonlinear (LN) models of retinal processing, and
78 several improvements over LN models have been proposed
79 for the identification of receptive fields (RF) (reviewed in

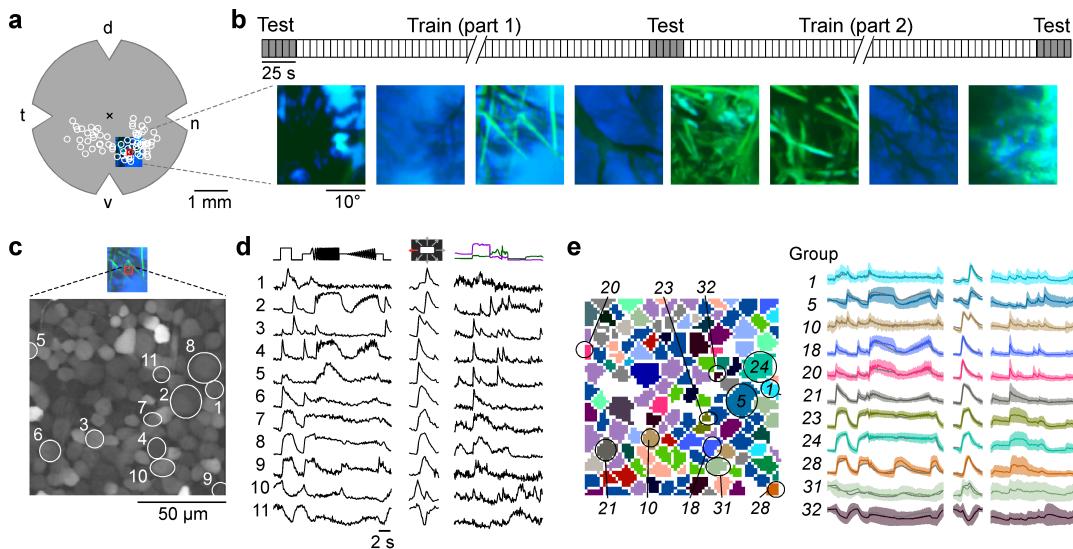


Figure 1. Mouse RGCs display diverse responses to a natural movie stimulus (a) Illustration of a flat-mounted retina, with recording fields (white circles) and stimulus area centred on the red recording field indicated (cross marks optic disc; d, dorsal; v, ventral; t, temporal; n, nasal). (b) Natural movie stimulus structure (top) and example frames (bottom). The stimulus consisted of 5-s clips taken from UV-green footage recorded outside (5), with 3 repeats of a 5-clip test sequence (highlighted in grey) and a 108-clip training sequence (see Methods). (c) Representative recording field (bottom; marked by red square in (a)) showing somata of ganglion cell layer (GCL) cells loaded with Ca^{2+} indicator OGB-1. (d) Ca^{2+} responses of exemplary RGCs (indicated by circles in (c)) to chirp (left), moving bar (centre), and natural movie (right) stimulus. (e) Same recording field as in (c) but with cells colour-coded by functional RGC group (left; see Methods and (6)) and group responses (coloured, mean \pm SD across cells; trace of example cells in (d) overlaid in black).

(24)). In recent years, convolutional neural network (CNN) models have become the state-of-the-art approach for predictive modelling of visual processing, both in the retina (25–28), as well as in higher visual areas (29–31). In the cortex, two recent studies took the CNN modelling approach further, beyond response prediction, by probing the networks for stimuli that would maximally excite the modelled neurons (32, 33). The resulting *maximally exciting inputs* (MEIs) were more complex and diverse than expected based on previous results obtained with synthetic stimuli and linear methods. Leveraging the power of this approach, another study highlighted the ethological relevance of colour by uncovering a state-dependent shift in chromatic preference of mouse V1 neurons, a shift that could facilitate the detection of aerial predators against a UV-bright sky (34).

Here, we combined the power of CNN-based modelling with large-scale recordings from RGCs to investigate colour processing in the mouse retina under natural stimulus conditions. Since mouse photoreceptors are sensitive to green and UV light (35), we recorded RGC responses to stimuli capturing the chromatic composition of natural mouse environments in these two chromatic channels. A model-guided search for MEIs in chromatic stimulus space predicted a novel type of chromatic tuning in transient Suppressed-by-Contrast (tSbC) RGCs, a type whose function is being debated (36–38).

A detailed *in-silico* characterisation followed up by experimental validation *ex-vivo* confirmed this cell type's pronounced and unique selectivity for dynamic full-field changes from green-dominated to UV-dominated scenes, a type of visual input that matches the scene statistics of transitions across the horizon (5, 39, 40). We therefore suggest a role for tSbC RGCs in detecting behaviourally relevant

changes in visual context, such as a transitions from ground (i.e. below the horizon) to sky (i.e. above the horizon).

Results

Here, we investigated colour processing in the mouse retina under natural stimulus conditions. To this end, we trained a CNN model on RGC responses to a movie covering both achromatic and chromatic contrasts occurring naturally in the mouse environment, and then performed a model-guided search for stimuli that maximise the responses of RGCs.

Mouse RGCs display diverse responses to a natural movie stimulus. Using two-photon population Ca^{2+} imaging, we recorded responses from 8,388 cells (in 72 recording fields across 32 retinae) in the ganglion cell layer (GCL) of the isolated mouse retina (Figure 1a) to a range of visual stimuli. Since complex interactions between colour channels have been mostly reported in the ventral retina and opsin-transitional zone, we focused our recordings on these regions (20, 21).

The stimuli included two achromatic synthetic stimuli – a contrast and frequency modulation (“chirp” stimulus) and a bright-on-dark bar moving in eight directions (“moving bar”, MB) – to identify the functional cell type (see below), as well as a dichromatic natural movie (Figure 1b-d). The latter was composed of footage recorded outside in the field using a camera that captured the spectral bands (UV and green; (5)) to which mouse photoreceptors are sensitive ($\lambda_{peak}^S = 360, \lambda_{peak}^M = 510$ nm for S- and M-cones, respectively (35)). We used 113 different movie clips, each lasting 5 s, that were displayed in pseudo-random order. Five of these constituted the test set and were repeated three times: at the beginning, in the middle and at the end of the movie

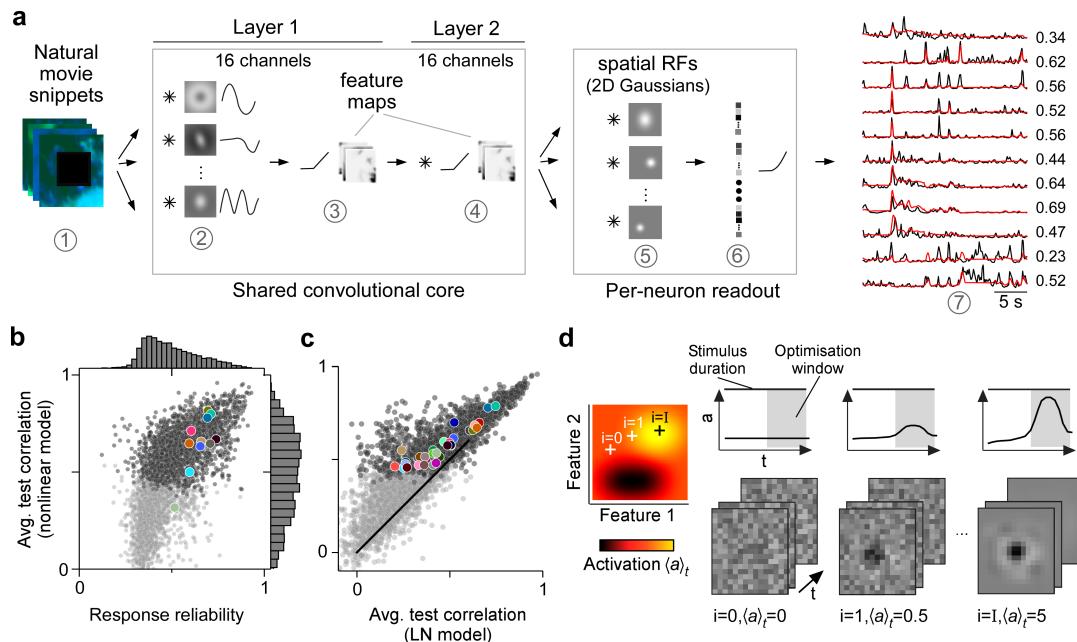


Figure 2. CNN model captures diverse tuning of RGC groups and predicts MEIs (a) Illustration of the CNN model and its output. The model takes natural movie clips as input (1), performs convolutions with 3D space-time separable filters (2) followed by a nonlinear activation function (3) in two consecutive layers (2-4) within its core, and feeds the output of its core into a per-neuron readout. For each RGC, the readout convolves the feature maps with a learned RF modelled as a 2D Gaussian (5), and finally feeds a weighted sum of the resulting vector through a softplus nonlinearity (6) to yield the firing rate prediction for that RGC (7). Numbers indicate averaged single-trial test set correlation between predicted (red) and recorded (black) responses. (b) Test set correlation between model prediction and neural response (averaged across three repetitions) as a function of response reliability (see Methods) for $N=3,527$ RGCs. Coloured dots correspond to example cells shown in Figure 1c-e. Dots in darker grey correspond to the $N=1,947$ RGCs that passed the model test correlation and movie response quality criterion (see Methods and Figure 1-figure supplement 1c). (c) Test set correlation (as in (b)) of model vs. test set correlation of a linearised version of the CNN model (for details, see Methods). Coloured dots correspond to RGC groups 1-32 (6). Dark and light grey dots as in (b). (d) Illustration of model-guided search for maximally exciting inputs (MEIs). The trained model captures neural tuning to stimulus features (far left; heat map illustrates “landscape” of neural tuning to stimulus features). Starting from a randomly initialised input (2nd from left; a 3D tensor in space and time; only one colour channel illustrated here), the model follows the gradient along the tuning surface (far left) to iteratively update the input until it arrives at the stimulus (bottom right) that maximises the model neuron’s activation within an optimisation time window (0.66 s, grey box, top right).

144 presentation, thereby allowing to assess the reliability of
145 neuronal responses across the recording (Figure 1b, top).

146 The responses elicited by the synthetic stimuli and the
147 natural movie were diverse, displaying ON (Figure 1d, rows
148 4-9), ON-OFF (row 3) and OFF (rows 1 and 2), as well
149 as sustained and transient characteristics (e.g., rows 8 and
150 4, respectively). Some responses were suppressed by
151 temporal contrast (generally, rows 10, 11; at high contrast and
152 frequency, row 9). A total of 6,984 GCL cells passed our
153 response quality criteria (see Methods); 3,527 cells could
154 be assigned to one of 32 previously characterised functional
155 RGC groups (6) based on their responses to the chirp and
156 moving bar stimuli using our recently developed classifier
157 (Figure 1e; Figure 1-figure supplement 1a) (5). Cells as-
158 signed to any of groups 33-46 were considered displaced
159 amacrine cells and were not analysed in this study (for de-
160 tailed filtering pipeline, see Figure 1-figure supplement 1c).

161 **CNN model captures diverse tuning of RGC groups**
162 **and predicts MEIs.** We trained a CNN model on the
163 RGCs’ movie responses (Figure 2a) and evaluated model
164 performance as the correlation between predicted and trial-
165 averaged measured test responses, $C(\hat{r}^{(n)}, \langle r^{(n)} \rangle_i)$ (Fig-
166 ure 2b). This metric can be interpreted as an estimate
167 of the achieved fraction of the maximally achievable cor-
168 relation (see Methods). The mean correlation per RGC
169 group ranged from 0.32 (G_{14}) to 0.79 (G_{24}) (Figure 1-figure

170 supplement 1b) and reached an average of 0.48 (for all
171 $N=3,527$ cells passing filtering steps 1-3, Figure 1-figure
172 supplement 1c). We also tested the performance of our
173 nonlinear model against a linearised version (see Methods;
174 equivalent to a Linear-Nonlinear (LN) model, and from here
175 on “LN model”) and found that the nonlinear CNN model
176 achieved a higher test set correlation for all RGC groups
177 (average correlation LN model: 0.38; G_{14} : 0.2, G_{24} : 0.65,
178 Figure 2c).

179 Next, we wanted to leverage our nonlinear CNN model
180 to search for potentially nonlinear stimulus selectivities of
181 mouse RGC groups. Towards this goal, we aimed to iden-
182 tify stimuli that optimally drive RGCs of different groups.
183 For linear systems, the optimal stimulus is equivalent to the
184 linear filter and can be identified with classical approaches
185 such as reverse correlation (41). However, since both the
186 RGCs and the CNN model were nonlinear, a different ap-
187 proach was necessary. Other recent modelling studies in
188 the visual system have leveraged CNN models to predict
189 static maximally exciting inputs (MEIs) for neurons in mon-
190 key V4 (33, 42) and mouse V1 (32, 34). We adopted this
191 approach to predict dynamic (i.e., time-varying) MEIs for
192 mouse RGCs. We used gradient ascent on a randomly ini-
193 tialised, contrast- and range-constrained input to find the
194 stimulus that maximised the mean activation of a given
195 model neuron within a short time window (0.66 s; see Meth-
196 ods; Figure 2d).

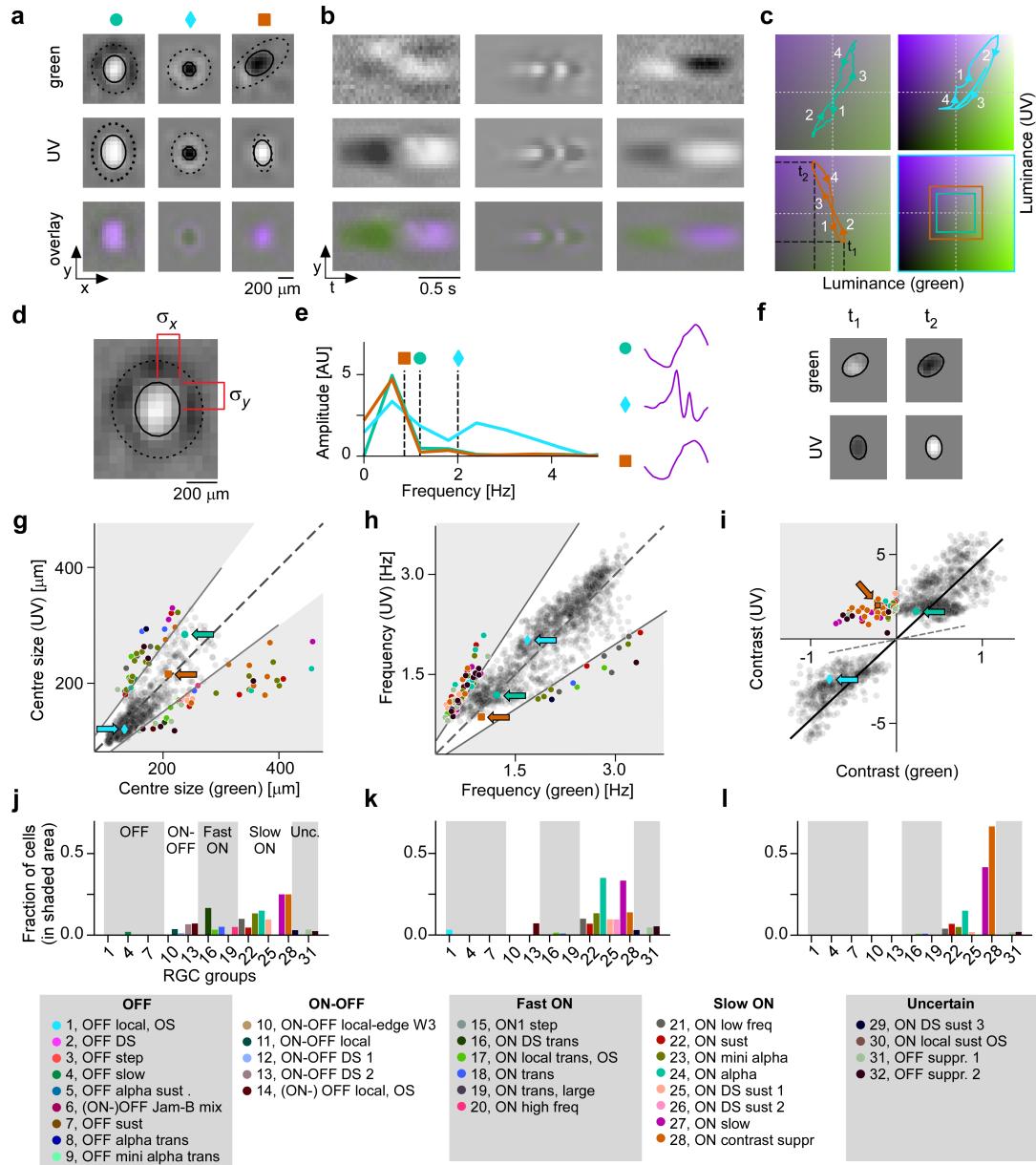


Figure 3. Spatial, temporal and chromatic properties of MEIs differ between RGC groups (a) Spatial component of three example MEIs for green (top), UV (middle) and overlay (bottom). Solid and dashed circles indicate MEI centre and surround fit, respectively. For display, spatial components s in the two channels were re-scaled to a similar range and displayed on a common grey-scale map ranging from black for $-\max(|s|)$ to white for $\max(|s|)$, i.e. symmetric about 0 (grey). (b) Spatio-temporal (y-t) plot for the three example MEIs (from (a)) at a central vertical slice for green (top), UV (middle) and overlay (bottom). Grey-scale map analogous to (a). (c) Trajectories through colour space over time for the centre of the three MEIs. Trajectories start at the origin (grey level); direction of progress indicated by arrow heads. Bottom right: Bounding boxes of the respective trajectory plots. (d) Calculation of MEI centre size, defined as $\sigma_x + \sigma_y$, with σ_x and σ_y the s.d. in horizontal and vertical direction, respectively, of the DoG fit to the MEI. (e) Calculation of MEI temporal frequency: Temporal components are transformed using Fast Fourier Transform, and MEI frequency is defined as the amplitude-weighted average frequency of the Fourier-transformed temporal component. (f) Calculation of centre contrast, which is defined as the difference in intensity at the last two peaks (indicated by t_1 and t_2 , respectively, in (c)). For the example cell (orange markers and lines), green intensity decreases, resulting in OFF contrast, and UV intensity increases, resulting in ON contrast. (g) Distribution of green and UV MEI centre sizes across $N=1,613$ cells (example MEIs from (a-c) indicated by arrows; symbols as shown on top of (a)). 95% of MEIs were within an angle of $\pm 8^\circ$ of the diagonal (solid and dashed lines); MEIs outside of this range are coloured by cell type. (h) As (g) but for distribution of green and UV MEI temporal frequency. 95% of MEIs were within an angle of $\pm 11.4^\circ$ of the diagonal (solid and dashed lines). (i) As (g) but for distribution of green and UV MEI centre contrast. MEI contrast is shifted away from the diagonal (dashed line) towards UV by an angle of 33.2° due to the dominance of UV-sensitive S-opsin in the ventral retina. MEIs at an angle $> 45^\circ$ occupy the upper left, colour-opponent ($\text{UV}^{\text{ON}}\text{-green}^{\text{OFF}}$) quadrant. (j, k) Fraction of MEIs per cell type that lie outside the angle about the diagonal containing 95% of MEIs for centre size and temporal frequency. Broad RGC response types indicated as in (6). (l) Fraction of MEIs per cell type in the upper-left, colour-opponent quadrant for contrast.

197 It is important to note that MEIs should not be con-
198 fused with or interpreted as the linear filters that result from
199 classical approaches (e.g., reverse correlation). This is be-
200 cause they result from an optimisation procedure that aims
201 at predicting the *optimal* stimulus for a cell. In fact, they
202 can differ significantly from linear filters, for example by
203 exhibiting more complexity and higher frequency compo-
204 nents (32).

205 **MEIs reflect known functional RGC group properties.**
206 The resulting MEIs were short, dichromatic movie clips;
207 their spatial, temporal, and chromatic properties and inter-
208 actions thereof are best appreciated in lower-dimensional vi-
209 sualisations (Figure 3a–c; more example MEIs in Figure 3-
210 figure supplement 1II).

211 To analyse the MEIs in terms of these properties, we
212 decomposed them into their spatial and temporal compo-
213 nents, separately for green and UV, and parameterised the
214 spatial component as a Difference-of-Gaussians (DoG) (40)
215 (N=1,613 out of 1,947, see Methods). We then located
216 MEIs along the axes in stimulus space corresponding to
217 three properties: centre size, mean temporal frequency, and
218 centre contrast, separately for green and UV (Figure 3d-f).
219 These MEI properties reflect RGC response properties clas-
220 sically probed with synthetic stimuli, such as spots of dif-
221 ferent sizes (8), temporal frequency modulations (6), and
222 stimuli of varying chromatic contrast (20, 21). Using the
223 MEI approach, we were able to reproduce known proper-
224 ties of RGC groups (Figure 3g-i). For example, sustained
225 ON α RGCs (G_{24}), which are known to prefer large stim-
226uli (6, 36), had MEIs with large centres (G_{24} , N=20 cells:
227 green centre size, mean \pm SD: $195 \pm 82 \mu\text{m}$; UV centre
228 size $178 \pm 45 \mu\text{m}$; average across all RGC groups: green
229 $148 \pm 42 \mu\text{m}$, UV $141 \pm 42 \mu\text{m}$; see Figure 3g).

230 The MEI's temporal frequency relates to the tempo-
231 ral frequency preference of an RGC: MEIs of G_{20} and
232 G_{21} , termed ON high frequency and ON low frequency
233 (6), had high and low average temporal frequency, respec-
234 tively (G_{20} , N=40 cells, green, mean \pm SD: $2.71 \pm 0.16 \text{ Hz}$,
235 UV $2.86 \pm 0.22 \text{ Hz}$; G_{21} , N=50 cells, green, mean \pm SD:
236 $2.32 \pm 0.63 \text{ Hz}$, UV $1.98 \pm 0.5 \text{ Hz}$; see Figure 3h). Some
237 MEIs exhibit fast oscillations (Figure 3e and Figure 3-figure
238 supplement 1II). This is not an artefact but rather a conse-
239 quence of optimising a stimulus to maximise activity over a
240 0.66 s time window (Figure 2d). To maximise the response
241 of a transient RGC over several hundred milliseconds, it has
242 to be stimulated repetitively, hence the oscillations in the
243 MEI. Maximising the response over a shorter time period
244 results in MEIs without oscillations (Figure 3-figure supple-
245 ment 2III).

246 Finally, the contrast of an MEI reflects what is tradi-
247 tionally called a cell's ON vs. OFF preference: MEIs of
248 ON and OFF RGCs had positive and negative contrasts, re-
249 spectively (Figure 3i). An ON-OFF preference can be in-
250 terpreted as a tuning map with two optima – one in the
251 OFF- and one in the ON-contrast regime. For an ON-
252 OFF cell, there are hence two stimuli that are approximately
253 equally effective at eliciting responses from that cell. Conse-

254 quently, for the ON-OFF RGC groups, optimisation resulted
255 in MEIs with ON or OFF contrast, depending on the rela-
256 tive strengths of the two optima and on the initial conditions
257 (Figure 3-figure supplement 1II, G_{10} , and see Discussion).

258 MEIs were also largely consistent within functional
259 RGC groups (Figure 3-figure supplement 1II). Where this
260 was not the case, the heterogeneity of MEIs could be at-
261 tributed to a known heterogeneity of cells within that group.
262 For example, MEIs of G_{31} RGCs were diverse (Figure 3-
263 figure supplement 1II), and the cells that were originally
264 grouped to form G_{31} probably spanned several distinct
265 types, as suggested by the group's unusually high coverage
266 factor (6). Together, these results provided strong evidence
267 that RGCs grouped based on responses to synthetic stimuli
268 (chirp and MB) also form functional groups in natural movie
269 response space.

270 **CNN model predicts centre colour-opponency in RGC**
271 **group G_{28} .** Our goal was to explore chromatic tuning of
272 RGCs and to identify novel stimulus selectivities related to
273 chromatic contrast. Therefore, we specifically focused on
274 regions in stimulus space where a given stimulus property
275 differs for green and UV. Therefore, for centre size and tem-
276 poral frequency, we asked, which RGC groups contributed
277 to the MEIs outside of the 95th percentile around the diag-
278 onal (Figure 3g,h,j,k). These 5% MEIs furthest away from the
279 diagonal were almost exclusively contributed by ON cells;
280 and among these, more so by slow than by fast ON cells.

281 MEI contrast needed to be analysed differently than
282 size and temporal frequency for two reasons. First, due to
283 the dominance of UV-sensitive S-opsin in the ventral retina
284 (17), stimuli in the UV channel were much more effective
285 at eliciting RGC responses. As a result, the contrast of most
286 MEIs is strongly shifted towards UV (Figure 3i). Second,
287 contrast in green and UV can not only vary along pos-
288 itive valued axes (as is the case for size and temporal fre-
289 quency), but can also take on opposite signs, resulting in
290 colour-opponent stimuli. Whereas most MEIs had the same
291 contrast polarity in both colour channels (i.e. both ON or
292 OFF, Figure 3c, blue and turquoise trajectories), some MEIs
293 had opposing contrast polarities in UV and green (Figure 3c,
294 orange trajectory, and Figure 3i, upper left quadrant). Thus,
295 for contrast, we asked which RGC groups contributed to
296 colour-opponent MEIs (i.e. MEIs in the colour-opponent,
297 upper left or lower right quadrant in Figure 3i). Again, slow
298 ON RGCs made up most of the cells with colour-opponent
299 MEIs. Here, G_{28} stood out: 66% (24/36) of all cells of this
300 group had colour-opponent MEIs (UV^{ON}-green^{OFF}), fol-
301 lowed by G_{27} with 42% colour-opponent MEIs.

302 The colour-opponency we found in G_{28} was not centre-
303 surround, as described before in mice (20), but rather a
304 centre-opponency (“co-extensive” colour-opponent RF; re-
305 viewed in (43)), as can be seen in the lower-dimensional
306 visualisations (Figure 3a,b, right column; 3c, orange trajec-
307 tory).

308 In conclusion, our model-guided *in-silico* exploration
309 of chromatic stimulus space revealed a variety of preferred
310 stimuli that captured known properties of RGC groups,

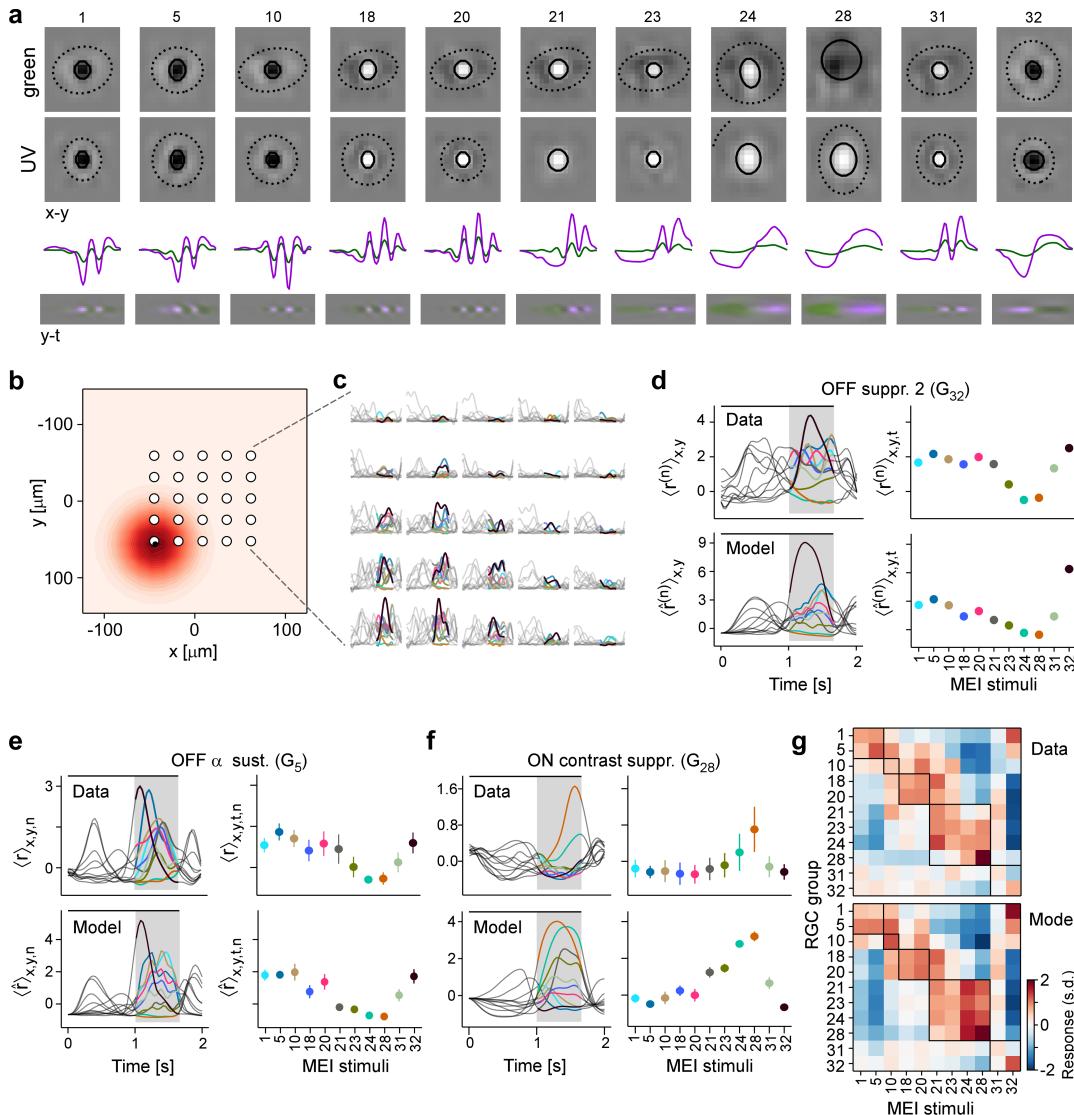


Figure 4. Experiments confirm MEIs predicted by model (a) MEIs shown during the experiment, with green and UV spatial components (top two rows), as well as green and UV temporal components (third row) and a spatio-temporal visualisation (fourth row). For display, spatial components s in the two channels were re-scaled to a similar range and displayed on a common grey-scale map ranging from black for $-\max(|s|)$ to white for $\max(|s|)$, i.e. symmetric about 0 (grey). Relative amplitudes of UV and green are shown in the temporal components. (b) Illustration of spatial layout of MEI experiment. White circles represent 5×5 grid of positions where MEIs were shown; red shading shows an example RF estimate of a recorded G_{32} RGC, with black dot indicating the RF centre position (Methods). (c) Responses of example RGC from (b) to the 11 different MEI stimuli at 25 different positions. (d) Recorded (top, $\langle r^{(n)} \rangle_{x,y,t}$) and predicted (bottom, $\hat{r}^{(n)}_{x,y,t}$) responses to the 11 different MEIs for example RGC n from (b, c). Left: responses are averaged across the indicated dimensions x, y (different MEI locations); black bar indicates MEI stimulus duration (from 0 to 1.66 s), grey rectangle marks optimisation time window (from 1 to 1.66 s). Right: Response to different MEIs, additionally averaged across time (t ; within optimisation time window). (e,f) Same as in (d), but additionally averaged across all RGCs (n) of G_5 ($N=6$) (e) and of G_{28} ($N=12$) (f). Error bars show SD across cells. (g) Confusion matrix, each row showing the z-scored response magnitude of one RGC group (averaged across all RGCs of that group) to the MEIs in (a). Confusion matrix for recorded cells (top; "Data") and for model neurons (bottom; "Model"). Black squares highlight broad RGC response types according to (6): OFF cells, ($G_{1,5}$) ON-OFF cells (G_{10}), fast ON cells ($G_{18,20}$), slow ON ($G_{21,23,24}$) and ON contrast suppressed (G_{28}) cells, and OFF suppressed cells ($G_{31,32}$).

and revealed a preference of G_{28} RGCs for centre colour-opponent, UV^{ON} -green OFF stimuli, a feature previously unknown for this RGC group.

Experiments confirm selectivity for chromatic contrast. Next, we verified experimentally that the MEIs predicted for a given RGC group actually drive cells of that group optimally. To this end, we performed new experiments in which we added to our battery of stimuli a number of MEIs chosen according to the following criteria: We wanted the MEIs to (i) span the response space (ON, ON- OFF , OFF, transient, sustained, and contrast-suppressed)

and (ii) to represent both well-described RGC types, such as α cells (i.e. $G_{5,24}$), as well as poorly understood RGC types, such as suppressed-by-contrast cells ($G_{28,31,32}$) (Figure 4a). We therefore chose MEIs of RGCs from groups G_1 (OFF local), G_5 (OFF α sustained), G_{10} (ON-OFF local-edge), G_{18} (ON transient), G_{20} (ON high frequency), G_{21} (ON low frequency), G_{23} (ON mini α), G_{24} (sustained ON α), G_{28} (ON contrast suppressed), G_{31} (OFF suppressed 1), and G_{32} (OFF suppressed 2). For simplicity, in the following we refer to the MEI of an RGC belonging to group g as group g 's MEI, or MEI g .

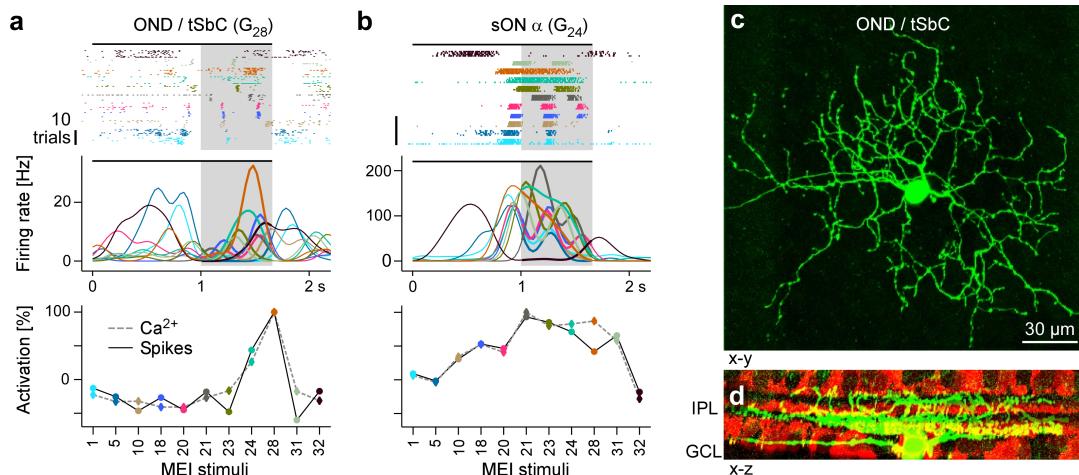


Figure 5. Electrical single-cell recordings of responses to MEI stimuli confirm chromatic selectivity of tSbC RGCs. (a) Spiking activity (top, raster plot; middle, firing rate) of a OND RGC in response to different MEI stimuli (black bar indicates MEI stimulus duration; grey rectangle marks optimisation time window, from 1 to 1.66 s). Bottom: Activation relative to mean as a function of MEI stimulus, averaged across cells (solid line, from electrical recordings, $N=4$; dashed line, from Ca^{2+} imaging, $N=11$ cells). Colours as in Figure 4. (b) Like (a) but for a sustained ON α cell (G_{24} ; $N=4$ cells, both for electrical and Ca^{2+} recordings). (c) Different ON delayed (OND/tSbC, G_{28}) RGC (green) dye-loaded by patch pipette after cell-attached electrophysiology recording (z-projection; x-y plane). (d) Cell from (c, green) as side-projection (x-z), showing dendritic stratification pattern relative to choline-acetyltransferase (ChAT) amacrine cells (tdTomato, red) within the inner plexiform layer (IPL).

We presented these MEIs on a regularly spaced 5×5 grid to achieve approximate centring of stimuli on RGC RFs in the recording field (Figure 4b,c). For these recordings, we fit models whose readout parameters allowed us to estimate the RGCs' RF locations. We used these RF location estimates to calculate a spatially weighted average of the responses to the MEIs displayed at different locations, weighting the response at each location proportional to the RF strengths at those locations (Figure 4b, red highlight, and Figure 4d, top). We then performed the same experiment *in-silico*, confirming that the model accurately predicts responses to the MEIs (Figure 4d, bottom; Figure 4-figure supplement 1IV). These experiments allowed us to evaluate MEI responses at the RGC group level (Figure 4e-f; Figure 3-figure supplement 1II).

We expected RGCs to show a strong response to their own group's MEI, a weaker response to the MEIs of functionally related groups, and no response to MEIs of groups with different response profiles. Indeed, most RGC groups exhibited their strongest ($G_{5,20,21,28,32}$) or second-strongest ($G_{1,10,23}$) response to their own group's MEI (Figure 4g, top). Conversely, RGC groups from opposing regions in response space showed no response to each others' MEIs (e.g. $G_{1,5}$ (OFF cells) vs. G_{21-28} (slow ON cells)). The model's predictions showed a similar pattern (Figure 4g, bottom), thereby validating the model's ability to generalise to the MEI stimulus regime.

Notably, G_{28} RGCs responded very selectively to their own MEI 28, displaying only weak responses to most other MEIs (Figure 4f,g, selectivity index G_{28} to MEI 28 $\text{SI}_{G_{28}}(28)$ defined as the average difference in response between MEI 28 and all other MEIs in units of standard deviation of the response, $\text{mean} \pm \text{SD}: 2.58 \pm 0.76$; see Methods). This was in contrast to other RGC groups, such as G_{23} and G_{24} , that responded strongly to MEI 28, but also to other MEIs from the slow ON response regime (Figure 4g, top;

Figure 4-figure supplement 1 IV, $\text{SI}_{G_{23}}(28)$, $\text{mean} \pm \text{SD}: 1.04 \pm 0.69$, $\text{SI}_{G_{24}}(28)$, $\text{mean} \pm \text{SD}: 1.01 \pm 0.46$). Hence, our validation experiments confirm the model's prediction that RGC group G_{28} is selective for centre colour-opponent, $\text{UV}^{\text{ON}}\text{-green}^{\text{OFF}}$ stimuli.

G₂₈ corresponds to the transient Suppressed-by-Contrast RGC type. Next, we sought to identify which RGC type G_{28} corresponds to. In addition to its unique centre colour opponency, the responses of G_{28} displayed a pronounced transient suppression to temporal contrast modulations (cf. chirp response in Figure 1e). Therefore, we hypothesised that G_{28} corresponds to the transient Suppressed-by-Contrast (tSbC) RGC type (37, 38, 44), which is one of three retinal SbC RGC types identified so far and is also referred to as ON delayed (OND) cell because of its delayed response onset (45).

To test this hypothesis, we performed cell-attached electrophysiology recordings (Figure 5) targeting tSbC/OND cells ($N=4$), identified by their responses to spots of multiple sizes (8), and later confirmed by their distinctive morphology ((45); type 73 in (9)) (Figure 5c,d). We recorded spikes while presenting the MEI stimuli (Figure 5a, top). Just like G_{28} RGCs in the Ca^{2+} imaging, tSbC/OND cells exhibited a pronounced selectivity for MEI 28, and were suppressed by most other MEIs (Figure 5a, middle and bottom). Notably, the characteristic delayed response onset was visible in both the Ca^{2+} (Figure 4f, top) and electrical (Figure 5a) responses but was not predicted by the model (Figure 4f, bottom).

As a control, we also recorded MEI responses of a different, well-characterised RGC type, sustained (s) ON α (G_{24} ; (46)) (Figure 5b, top; $N=4$). Again, the electrical recordings of the cells' MEI responses yielded virtually the same results as the Ca^{2+} imaging (Figure 5b, middle and bottom; cf. Figure 4-figure supplement 1IV). Crucially, sON α cells were not selective for MEI 28. The fact that

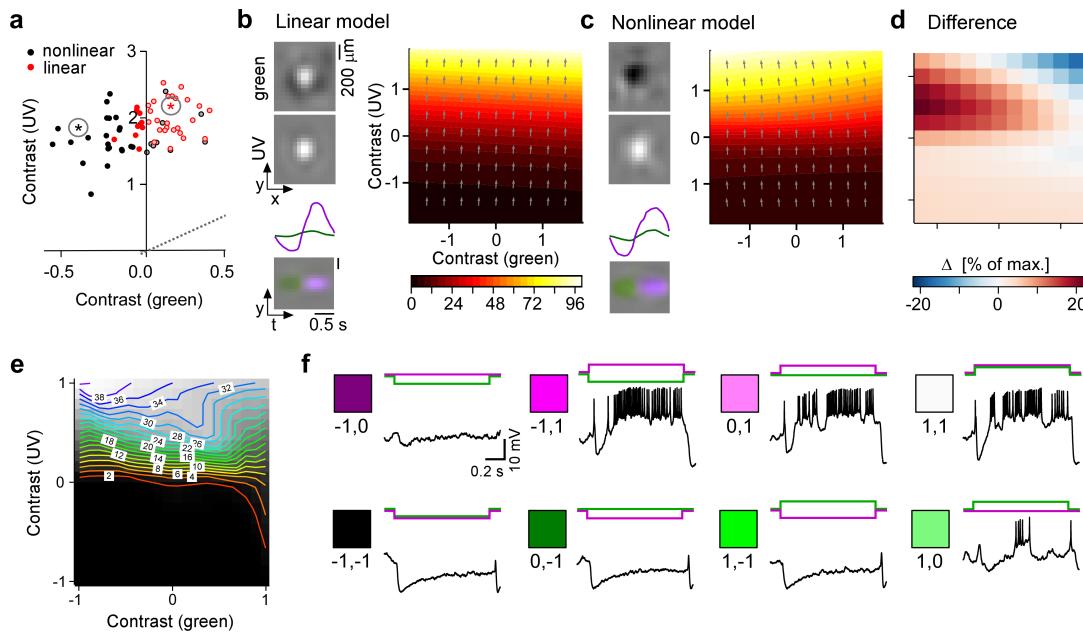


Figure 6. Chromatic contrast selectivity of G₂₈ RGCs derives from a nonlinear transformation of stimulus space (a) Distribution of green and UV MEI centre contrast for a linear-nonlinear (LN) model (red) and a nonlinear CNN model (black). Colour-opponent cells highlighted by filled marker. (b,c) Left: MEIs for an example cell of RGC group G₂₈, generated with the LN model (b) or the CNN model (c). The cell's MEI centre contrast for both models is marked in (a) by asterisks. Right: Respective tuning maps of example model neuron in chromatic contrast space. Colours represent responses in % of maximum response; arrows indicate the direction of the response gradient across chromatic contrast space. (d) Difference in response predicted between LN and CNN model (in % of maximum response). (e) Contour plot of activity vs. green and UV contrast for an example tSbC (G₂₈) RGC measured in whole-cell current-clamp mode. Labels on the contour plot indicate spike count along isoresponse curves. (f) Traces are examples of responses at the 8 extremes of -100%, 0, or 100% contrast in each colour channel.

405 these experiments with precise positioning of stimuli on the
406 cells' RFs elicited the same responses as the 2P experiments
407 confirms the validity of the grid-approach for stimulus pre-
408 sentation used in the latter.

409 **Chromatic contrast selectivity derives from a nonlin-
410 ear transformation of stimulus space.** Next, we asked
411 whether G₂₈ (tSbC) RGC's selectivity is a linear feature, as
412 could be achieved by two linear filters with opposite signs
413 for the two colour channels, or whether it is a nonlinear
414 feature. To address this question, we tested whether an
415 LN model (implemented using convolutions; see Methods)
416 could recover the chromatic selectivity of G₂₈ by predicting
417 MEIs using the LN model (Figure 6). We found that the
418 LN model predicted colour-opponent MEIs for only 9 out
419 of 36 (25%) G₂₈ RGCs (nonlinear CNN: 24 out of 36 (66%)
420 colour-opponent MEIs; Figure 6a-c). This finding argues
421 against the possibility that G₂₈'s colour opponency can be
422 explained on the computational level by two opposite-sign
423 linear filters operating on the two colour channels, which
424 could be recovered by a LN model. Instead, it suggests the
425 presence of a nonlinear dependency between chromatic con-
426 trast (of the stimulus) and chromatic selectivity (of the cell).
427 In other words, G₂₈ RGCs process stimuli differently de-
428 pending on their chromatic contrast, a nonlinear feature that
429 cannot be accurately captured by a LN model that makes
430 a single estimate of the linear filter for the whole stimulus
431 space.

432 To understand the nature of this dependency, we ex-
433 panded the estimate of the model RGCs' tuning to colour
434 contrast around the maximum (the MEI). We did this by

435 mapping the model neurons' response and its gradient in 2D
436 chromatic contrast space (Figure 6c). This analysis revealed
437 that, indeed, G₂₈ RGCs have a nonlinear tuning for colour
438 contrast: they are strongly UV-selective at lower contrasts,
439 but become colour-opponent, i.e. additionally inhibited by
440 green, for higher contrasts. For individual neurons with very
441 strong colour opponency that extends over a large region of
442 chromatic contrast space, also the LN model's approxima-
443 tion reflects this colour opponency, which demonstrates that
444 the LN model can in principle model colour opponency, too
445 (Figure 5-figure supplement 1V). We confirmed the model's
446 predictions about G₂₈'s nonlinear tuning for colour contrast
447 experimentally by electrically recording from morpholog-
448 ically identified G₂₈ (tSbC) RGCs (Figure 6e,f). The ex-
449 ample cell shown in the figure exhibits the same nonlinear
450 tuning in chromatic contrast space, with the firing rate (Figure
451 6f) and, consequently, the tuning curve (Figure 6e) peak-
452 ing for UV^{ON}-green^{OFF} stimuli.

453 The nonlinearity in tuning to colour contrast of G₂₈
454 RGCs leads to a warping of stimulus space (Figure 6) that
455 amplifies the distance of colour-opponent stimuli from non-
456 colour-opponent stimuli and thereby increases their discrim-
457 inability. We therefore hypothesised that the representation
458 of visual input formed by G₂₈ might serve to detect an etho-
459 logically relevant, colour-opponent feature from the visual
460 scene. What may be this feature?

461 **Warped representation allows for detection of
462 ground-to-sky transitions.** Studies analysing visual
463 scenery from the mouse's perspective have repeatedly
464 found that chromatic contrast changes strongly at the

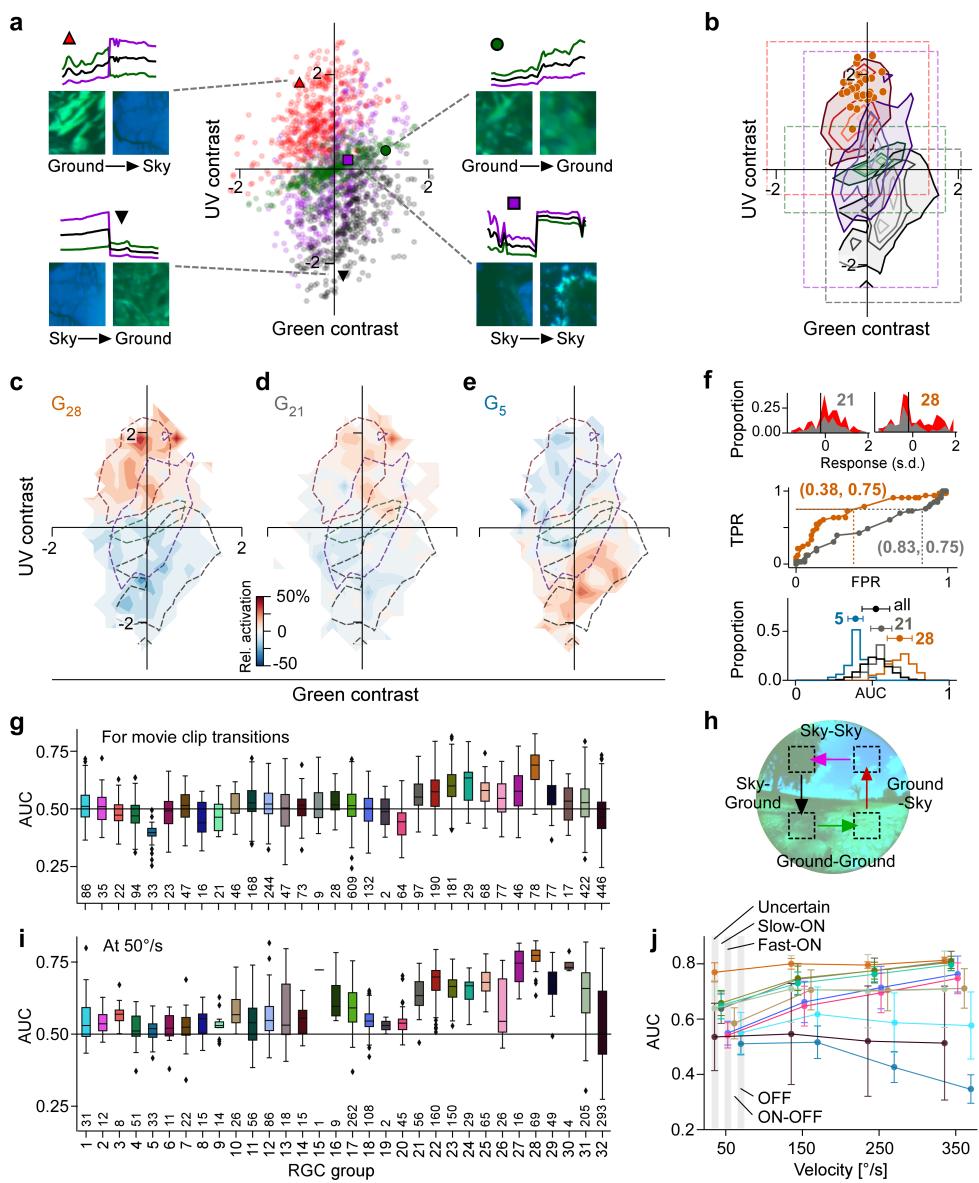


Figure 7. Chromatic contrast tuning allows detection of ground-to-sky transitions (a) Distribution of green and UV contrasts of all movie inter-clip transitions (centre), separately for the 4 transition types, for each of which an example is shown: ground-to-sky ($N=525$, top left, red triangle), ground-to-ground ($N=494$, top right, green circle), sky-to-ground ($N=480$, bottom left, black downward triangle), and sky-to-sky ($N=499$, bottom right, purple square). Images show last and first frame of pre- and post-transition clip, respectively. Traces show mean full-field luminance of green and UV channels in last and first 1 s of pre- and post-transition clip. Black trace shows luminance averaged across colour channels. (b) Distributions as in (a), but shown as contours indicating isodensity lines of inter-clip transitions in chromatic contrast space. Density of inter-clip transitions was estimated separately for each type of transition from histograms within 10×10 bins that were equally spaced within the coloured boxes. Four levels of isodensity for each transition type shown, with density levels at 20 % (outermost contour, strongest saturation), 40 %, 60 % and 80 % (innermost contour, weakest saturation) of the maximum density observed per transition: 28 sky-to-ground (black), 75 ground-to-ground (green), 42 sky-to-sky (purple) and 45 ground-to-sky (red) transitions per bin. Orange markers indicate locations of $N=36$ G_{28} MEIs in chromatic contrast space (cf. Figure 3i). (c) Tuning map of G_{28} RGCs ($N=78$), created by averaging the tuning maps of the individual RGCs, overlaid with outermost contour lines from (b) (cf. Figure 6-figure supplement 2VIIb). (d,e) Same as (c) for G_{21} ((g), $N=97$) and G^5 ((h), $N=33$). (f) Top: Illustration of ROC analysis for two RGCs, a G_{21} (left) and a G_{28} (right). For each RGC, responses to all inter-clip transitions were binned, separately for ground-to-sky (red) and all other transitions (grey). Middle: Sliding a threshold d across the response range, classifying all transitions with response $> d$ as ground-to-sky, and registering the false-positive-rate (FPR) and true-positive-rate (TPR) for each threshold yields an ROC curve. Numbers in brackets indicate (FPR, TPR) at the threshold indicated by vertical line in histograms. Bottom: Performance for each cell, quantified as area under the ROC curve (AUC), plotted as distribution across AUC values for all cells (black), G_{21} (grey), G^5 (blue), and G_{28} (orange); AUC mean \pm SD indicated as dots and horizontal lines above histograms. (g) Boxplot of AUC distributions per cell type. The box extends from the first quartile (Q_1) to the third quartile (Q_3) of the data; the line within a box indicates the median. The whiskers extend to the most extreme points still within $[Q_1 - 1.5 \times \text{IQR}, Q_3 + 1.5 \times \text{IQR}]$, IQR = inter-quartile range. Diamonds indicate points outside this range. All elements of the plot (upper and lower boundaries of the box, median line, whiskers, diamonds) correspond to actual observations in the data. Numbers of RGCs for each type are indicated in the plot. (h) Illustration of stimulus with transitions as in (a) but at different velocities (50, 150, 250, and 350 ms). (i) Like (g) but for model cells and transition movies from (h) at 50 %. (j) AUC as function of transition velocity for example RGC groups ($G_{(1,5)}, (10), (18,20), (21, 23, 24), (28, 31, 32)$).

465 horizon (5, 21, 39, 40). G₂₈ RGCs are selective to this
466 kind of change in chromatic contrast: their MEI consists
467 of a spatially extensive and sustained change in luminance
468 from green to UV. We hypothesised that this change in
469 chromatic contrast might serve as a proxy for detecting
470 changes in visual context, as might be elicited when a cell's
471 RF transitions across the horizon. Such transitions could
472 be caused by head or eye movements, and detecting this
473 change in visual context (i.e. ground vs. sky) may help
474 interpreting signals in other RGC channels.

475 To test if G₂₈ (tSbC) RGCs respond to such a stimulus,
476 we used the transitions between movie clips (*inter-clip*
477 transitions; cf. Figure 1b) as a proxy for the type of visual
478 input elicited by head or eye movements: ground-to-ground
479 and sky-to-sky transitions for horizontal movements without
480 change in visual context, and ground-to-sky and sky-to-
481 ground transitions for vertical movements with a change in
482 visual context. We then calculated the contrast of these trans-
483 itions in the green and UV channel and mapped them to the
484 chromatic contrast stimulus space (Figure 7a). We found
485 that ground-to-ground and sky-to-sky transitions were dis-
486 tributed along the diagonal, whereas the two transitions re-
487 sembling visual input elicited by vertical movements cross-
488 ing the horizon fell into the two colour-opponent quadrants:
489 sky-to-ground transitions in the lower right quadrant, and
490 ground-to-sky transitions in the upper left quadrant (Figure
491 7a,b). The UV^{ON}-green^{OFF} MEIs 28 share a location
492 in stimulus space with ground-to-sky transitions in terms of
493 chromatic contrast (cf. Fig 3i).

494 Do G₂₈ RGCs indeed respond strongly to visual con-
495 text changes as occur in ground-to-sky transitions, i.e. to the
496 “naturally occurring version” of their MEIs? To address this
497 question, we extracted the RGC responses to the inter-clip
498 transitions, thereby mapping out their tuning across chro-
499 matic contrasts (Figure 6-figure supplement 1VI, Figure 6-
500 figure supplement 6VIIb), and then averaged the resulting
501 single-cell tuning maps for each RGC group (for exam-
502 ples, see Figure 7c-e). G₂₈ is most strongly tuned to full-
503 field transitions in the upper left quadrant containing mostly
504 ground-to-sky inter-clip transitions (Figure 7c) – unlike, for
505 example, non-colour-opponent reference RGC groups from
506 the slow ON and OFF response regime (Figure 7d,e).

507 Could a downstream visual area detect ground-to-sky
508 visual context changes based on input from G₂₈ RGCs? To
509 answer this question, we performed a linear detection analy-
510 sis for each RGC by sliding a threshold across its responses
511 to the inter-clip transitions, classifying all transitions that
512 elicited an above-threshold response as ground-to-sky, and
513 evaluating false-positive and true-positive rates (FPR and
514 TPR, respectively) for each threshold (Figure 7f). Plotting
515 the resulting TPRs for all thresholds as a function of FPRs
516 yields a receiver operating characteristic (ROC) curve (47)
517 (Figure 7f, middle). The area under this curve (AUC) can
518 be used as a measure of detection performance: it is equiv-
519 alent to the probability that a given RGC will respond more
520 strongly to a ground-to-sky transition than to any other type
521 of transition. Indeed, G₂₈ RGCs achieved the highest AUC

522 on average (Figure 7f, bottom, and g; G₂₈, mean \pm SD AUC
523 (N=78 cells): 0.68 ± 0.08 ; two-sample permutation test G₂₈
524 vs. all other groups with at least N=4 cells (see Methods),
525 significant for each group, with $\alpha = 0.0017$ Bonferroni-
526 corrected for 30 multiple comparisons).

527 Ground-to-sky transitions and, therefore visual context
528 changes, can also appear in the lower visual field, that is,
529 on the dorsal retina, where RGCs receive weaker UV input
530 (20). Therefore, we recorded additional fields in the dor-
531 sal retina (Figure 6-figure supplement 2VIIa) and found also
532 here that G₂₈ (tSbC) RGCs displayed the strongest tuning to
533 ground-to-sky transitions among all dorsal RGCs (Figure 6-
534 figure supplement 2VIIc-h, for statistics, see legends).

535 Visual context changes triggered by different beh-
536 viourisms, such as locomotion and head or eye movements
537 will differ strongly with respect to their statistics – in partic-
538 ular with respect to their speed. Therefore, for G₂₈ (tSbC)
539 RGCs to play a role in detecting context changes, their de-
540 tection performance should be robust across velocities. To
541 test whether this is the case, we conducted additional *in-
542 silico* experiments where we predicted responses of all RGC
543 groups to stimuli simulating transitions across the visual
544 field with and without context change (Figure 7h) at differ-
545 ent velocities: 50, 150, 250, and 350 visual degrees per sec-
546 ond (°/s; see Methods; Figure 6-figure supplement 3VIIIa,b)
547 The slowest speed simulated visual input as could be elicited
548 by locomotion, and the fastest speed approached that of sac-
549 cades (48). We then performed an ROC analysis on the
550 model cell responses, which confirmed that G₂₈ RGCs could
551 distinguish ground-to-sky context changes from all other
552 types of transitions robustly across different speeds (Figure
553 7i,j). Interestingly, the advantage of G₂₈ over other RGC
554 groups in performing this detection task diminished with in-
555 creasing speed (Figure 6-figure supplement 3VIIIc,d); see
556 also Discussion).

557 Together, these analyses demonstrate that a down-
558 stream area, reading out from a single RGC group, would
559 achieve the best performance in detecting ground-to-sky
560 context changes if it based its decisions on inputs from G₂₈
561 RGCs, robustly across different lighting conditions (transi-
562 tions between movie snippets), retinal location (ventral and
563 dorsal), and speeds. Since such an area would receive input
564 not from a single cell, but from a local population of cells,
565 the detection performance of single cells should represent a
566 lower bound to that area's detection performance.

567 Discussion

568 We combined large-scale recordings of RGC responses to
569 natural movie stimulation with CNN-based modelling to in-
570 vestigate colour processing in the mouse retina. By search-
571 ing the stimulus space *in silico* to identify *most exciting*
572 *inputs* (MEIs), we found a novel type of chromatic tuning
573 in tSbC RGCs. We revealed this RGC type's pronounced
574 and unique selectivity for full-field changes from green-
575 dominated to UV-dominated scenes, a stimulus that matches
576 the chromatic statistics of ground-to-sky transitions in natu-
577 ral scenes. Therefore, we suggest that tSbC cells may signal

578 context changes within their RF. Beyond our focus on tSbC
579 cells, our study demonstrates the utility of an *in silico* ap-
580 proach for generating and testing hypotheses about the etho-
581 logical relevance of sensory representations.

582 **Nonlinear approaches for characterising neuronal**
583 **selectivities and invariances.** We leverage image-
584 computable models in combination with an optimisation
585 approach to search in dynamic, chromatic stimulus space
586 for globally optimal inputs for RGCs, the MEIs. The result-
587 ing MEI represents the peak in the nonlinear loss landscape
588 that describes the neuron's tuning in high-dimensional
589 stimulus space. This approach has also been used to reveal
590 the complexities and nonlinearities of neuronal tuning in
591 monkey visual cortex area V4 (33, 42) and mouse area V1
592 (32, 34). Still, these approaches are not the "silver bullet"
593 for identifying nonlinear selectivities. One important
594 limitation is that searching for the *most* exciting input will
595 return a single input – even when there are several inputs
596 that would elicit equal response, such as ON and OFF
597 stimuli for ON-OFF cells (see Figure II, G₁₀ MEIs). A
598 remedy for this limitation is to search for *diverse* exciting
599 inputs by generating stimuli that are both highly effective at
600 eliciting neural responses and at the same time distinct from
601 one another. Ding et al. (49) used this approach to study
602 bipartite invariance in mouse V1 (see also (50)). Related to
603 this, Goldin et al. (51) searched for locally optimal stimulus
604 perturbations for mouse RGCs and found that the selectivity
605 for positive or negative contrast in a subset of cells is
606 context-dependent. These cells signal absolute contrast, i.e.
607 they are invariant to contrast polarity ("classical" ON vs.
608 OFF). Together, these studies showcase the versatility of the
609 toolkit of optimisation-based approaches at characterising
610 nonlinear neuronal operations in high-dimensional, natural
611 stimulus spaces. We add to this toolkit by first searching
612 for a globally optimal stimulus, and then searching locally
613 in its vicinity to map the cells' loss landscape around the
614 maximum.

615 **Circuit mechanisms for colour opponency in tSbC**
616 **RGCs.** Most previous studies of colour opponency in the
617 mouse retina have identified sparse populations of colour-
618 opponent RGCs that have not been systematically assigned
619 to a particular functional type (20, 21, 52). The only studies
620 that have examined the mechanisms of colour opponency in
621 identified mouse RGC types showed a centre-surround orga-
622 nisation, with RF centre and surround having different
623 chromatic preferences ((18, 53); and (54), but see (55)).
624 While we do not specifically analyse centre-surround op-
625 ponency in this study, we see a similar trend as described
626 previously in many RGC types, with stronger surrounds
627 in the green channel relative to the UV channel (see Figure
628 4a, Figure 3-figure supplement 1II). tSbC RGCs, in
629 contrast, respond to spatially co-extensive colour-opponent
630 stimuli, functionally reminiscent of colour-opponent RGCs
631 in Guinea pig (56) and ground squirrels (57).

632 In mice, centre-surround opponency has been at-
633 tributed to the opsin gradient (53) and rod contributions in

634 the outer retina (18, 20), whereas the circuitry for spatially
635 co-extensive opponency remains unknown. It seems un-
636 likely, though, that the opsin gradient plays a major role
637 in the tSbC cell's colour opponency, because both ventral
638 and dorsal tSbC cells preferentially responded to full-field
639 green-to-UV transitions. In primates, spatially co-extensive
640 colour opponency in small bistratified RGCs is thought to
641 arise from the selective wiring of S-ON and M/L-OFF bi-
642 polar cells onto the inner and outer dendritic strata, respec-
643 tively ((58), but see (59)). A similar wiring pattern seems
644 unlikely for tSbC RGCs, since their inner dendrites do not
645 co-stratify with the S-ON (type 9) bipolar cells, nor do their
646 outer dendrites co-stratify with the candidate M-OFF bi-
647 polar cell (type 1) (60). The bistratified dendritic arbour distin-
648 guishes the mouse tSbC also from the colour-opponent ON
649 RGC type in Guinea pig, which is monostratified (56).

650 The large RF centres of the tSbC cells, extending well
651 beyond their dendritic fields, come from a non-canonical cir-
652 cuit, in which tonic inhibition onto the RGC via GABA_B
653 receptors is relieved via serial inhibition from different
654 amacrine cells using GABA_C receptors (36). An intriguing
655 possibility is that a colour-selective amacrine cell is part of
656 this circuit, perhaps supporting chromatically tuned disinhi-
657 bition in the absence of selective wiring from the aforemen-
658 tioned cone-selective bipolar cells onto the RGC.

659 **A new functional role for tSbC RGCs.** Suppressed-by-
660 contrast responses have been recorded along the early visual
661 pathway in dorsal lateral geniculate nucleus (dLGN), su-
662 perior colliculus (SC), and primary visual cortex (V1) (61–63),
663 with their function still being debated (64). In the retina,
664 three types of SbC RGCs have so far been identified (re-
665 viewed in (45)), among them the tSbC cell (36–38). De-
666 spite their relatively recent discovery, tSbC RGCs have been
667 suggested to play a role in several different visual computa-
668 tions. The first report of their light responses in mice con-
669 nected them to the SbC RGCs previously discovered in rab-
670 bit, cat, and macaque, and suggested a role in signalling self-
671 generated stimuli, perhaps for saccade suppression (37).
672 Aided by a new intersectional transgenic line to selectively
673 label tSbC RGCs (38), their projections were traced to areas
674 in SC, v- and dLGN, and nucleus of the optic tract (NOT).
675 The latter stabilises horizontal eye movements; however, as
676 the medial terminal nucleus (MTN), which serves stabilisa-
677 tion of vertical eye movements, lacks tSbC innervation, it
678 is unclear whether and how these RGCs contribute to gaze
679 stabilisation.

680 A retinal study identified the circuit mechanisms re-
681 sponsible for some of the unique spatial and temporal re-
682 sponse properties of tSbC cells and suggested a possible role
683 in defocus detection to drive emmetropization in growing
684 eyes and accommodation in adults (36, 65). Here, we iden-
685 tified another potential role for these RGCs in vision based
686 on the chromatic properties of their RFs: signalling visual
687 context changes (see next section). These different possible
688 functional roles are not mutually exclusive, and might even
689 be complementary in some cases, highlighting the difficulty
690 in assigning single features to distinct RGC types (16). In

particular, the centre colour-opponency that we discovered in tSbC RGCs could serve to enhance their role in defocus detection by adding a directional signal (myopic vs. hyperopic) based on the chromatic aberration of lens and cornea (66). Future studies may test these theories by manipulating these cells *in vivo* using the new transgenic tSbC mouse line (38).

Behavioural relevance of context change detection. The horizon is a prominent landmark in visual space: it bisects the visual field into two regions, ground and sky. This is particularly relevant in animals like mice, where eye motion largely accounts for head movements and keeps the visual field stable with respect to the horizon (48). Visual stimuli carry different meaning depending on where they occur relative to the horizon, and context-specific processing of visual inputs is necessary for selecting appropriate behavioural responses (reviewed in (67)). For example, it is sensible to assume that a looming stimulus above the horizon is a predator, the appropriate response to which would be avoidance (that is, escape or freezing). A similar stimulus below the horizon, however, is more likely to be harmless or even prey. To allow for time-critical perceptual decisions – predator or prey – and corresponding behavioural response selection – avoidance or approach – it might be useful that stimulus (e.g., dark moving spot) and contextual information converge soon in the visual circuitry. Notably, VGluT3-expressing amacrine cells (a “hub” for distributing information about motion) represent a shared element in upstream circuitry, providing opposite-sign input to tSbC and to RGCs implicated in triggering avoidance behaviour, such as tOFF α (13, 46) and W3 cells (68). In downstream circuitry, SbC inputs have been found to converge with “conventional” RGC inputs onto targets in dLGN and NOT; whether tSbC axons specifically converge with tOFF α or W3 axons remains to be tested. Such convergence may allow “flagging” the activity of these RGCs with their local context (sky/threat or ground/no threat).

Depending on the behaviour that elicits a context change – be it a head or eye movement or locomotion – the parameters of the incoming stimulus, such as illumination level and velocity, may change. To be behaviourally useful, a context-change-flagging signal needs to be reliable and robust across these different stimulus parameters. While many slow-ON RGCs achieve high detection performance at higher transition velocities, probably reacting to the increasingly flash-like stimuli, tSbC RGCs were the only type with robustly high performance across different levels of illumination and all simulated speeds.

In-silico approaches to linking neural tuning and function. The modelling of retinal responses to natural stimuli has advanced our understanding of the complexity of retinal processing in recent years. As suggested in a recent review, it is helpful to consider the contributions of different studies in terms of one of three perspectives on the retinal encoding of natural scenes: The circuit perspective (“how?”), the normative perspective (“why?”), and the cod-

ing perspective (“what?”) (69). For example, an *in-silico* dissection of a CNN model of the retina offered explanations on how the surprisingly complex retinal computations, such as motion reversal, omitted stimulus response, and polarity reversal, emerge from simpler computations within retinal circuits (26, 27). Taking on the normative perspective, anatomically constrained deep CNNs trained on image recognition suggested a dependency between the complexity of retinal representations and the computational power of downstream cortical networks: Whereas a computationally powerful cortex, as found in primates, can deal with faithful, linear representations of visual inputs, a simpler cortical circuitry, as found in mice, requires more complex feature extraction upstream in the retina ((70, 71); but see (72)). However, the full potential of CNN models as tools for understanding sensory processing goes beyond response prediction and reproducing effects that are already described in the literature.

Here, we developed an approach that allows investigating the complexity of retinal processing simultaneously from the coding and the normative perspectives: A global search for most exciting mouse RGC inputs in dynamic, chromatic stimulus space answers the question of *what* it is that retinal neurons encode. Interpreting the abstract features extracted by the retina against the backdrop of natural stimulus space points to *why* these features might be behaviourally relevant. And finally, classifying individual RGCs into types then allows to bring in the circuit perspective through targeted experiments aimed at dissecting *how* specific retinal computations are implemented.

Methods

Animals and tissue preparation. All imaging experiments were conducted at the University of Tübingen; the corresponding animal procedures were approved by the governmental review board (Regierungspräsidium Tübingen, Baden-Württemberg, Konrad-Adenauer-Str. 20, 72072 Tübingen, Germany) and performed according to the laws governing animal experimentation issued by the German Government. All electrophysiological experiments were conducted at Northwestern University; the corresponding animal procedures were performed according to standards provided by Northwestern University Center for Comparative Medicine and approved by the Institutional Animal Care and Use Committee (IACUC).

For all imaging experiments, we used 4- to 15-week-old C57Bl/6 J mice (n=23; JAX 000664) of either sex (10 male, 13 female). These animals were housed under a standard 12 h day/night rhythm at 22° and 55% humidity. On the day of the recording experiment, animals were dark-adapted for at least 1 h, then anaesthetised with isoflurane (Baxter) and killed by cervical dislocation. All following procedures were carried out under very dim red (> 650 nm) light. The eyes were enucleated and hemisected in carboxygenated (95% O₂, 5% CO₂) artificial cerebrospinal fluid (ACSF) solution containing (in mM): 125 NaCl, 2.5 KCl, 2 CaCl₂, 1 MgCl₂, 1.25 NaH₂PO₄, 26 NaHCO₃, 20 glu-

803 cose, and 0.5 L-glutamine at pH 7.4. Next, the retinae were
804 bulk-electroporated with the fluorescent Ca^{2+} indicator Oregon-Green BAPTA-1 (OGB-1), as described earlier (73).
805 In brief, the dissected retina was flat-mounted onto an Anodisc (#13, 0.2 μm pore size, GE Healthcare) with the RGCs
806 facing up, and placed between a pair of 4-mm horizontal
807 plate electrodes (CUY700P4E/L, Nepagene/Xceltis). A 10- μl drop of 5 mM OGB-1 (hexapotassium salt; Life Technologies)
808 in ACSF was suspended from the upper electrode
809 and lowered onto the retina. Next, nine pulses ($\approx 9.2\text{ V}$,
810 100 ms pulse width, at 1 Hz) from a pulse generator/wide-
811 band amplifier combination (TGP110 and WA301, Thurlby
812 handar/Farnell) were applied. Finally, the tissue was placed
813 into the microscope's recording chamber, where it was per-
814 fused with carboxygenated ACSF (at $\approx 36^\circ\text{C}$) and left to
815 recover for ≥ 30 min before recordings started. To visualise
816 vessels and damaged cells in the red fluorescence
817 channel, the ACSF contained $\approx 0.1\text{ }\mu\text{M}$ Sulforhodamine-
818 101 (SR101, Invitrogen) (74). All procedures were carried
819 out under dim red ($> 650\text{ nm}$) light.

820 For electrophysiology experiments, we used ChAT-Cre
821 (JAX 006410) x Ai14 (JAX 007914) mice on a C57Bl/6J
822 background ($n=2$, male, aged 27 and 30 weeks). Mice were
823 housed with siblings in groups up to 4, fed normal mouse
824 chow and maintained on a 12:12 h light/dark cycle. Be-
825 fore the experiment, mice were dark-adapted overnight and
826 sacrificed by cervical dislocation. Retinal tissue was iso-
827 lated under infrared illumination (900 nm) with the aid
828 of night-vision goggles and IR dissection scope attach-
829 ments (BE Meyers). Retinal orientation was identified us-
830 ing scleral landmarks (75), and preserved using relieving
831 cuts in cardinal directions, with the largest cut at the dor-
832 sal retina. Retinas were mounted on 12mm poly-D-lysine
833 coated glass affixed to a recording dish with grease, with
834 the GCL up. Oxygenation was maintained by superfusing
835 the dish with carboxygenated Ames medium (US Bi-
836 ological, A1372-25) warmed to 32°C . For cell-attached
837 single cell recordings, we used Symphony software (<https://symphony-das.github.io/>) with custom extensions (<https://github.com/Schwartz-AlaLaurila-Labs/sa-labs-extension>).

838 Owing to the exploratory nature of our study, we did
839 not use randomisation and blinding. No statistical methods
840 were used to predetermine sample size.

841 **Two-photon calcium imaging.** We used a MOM-type
842 two-photon microscope (designed by W. Denk; pur-
843 chased from Sutter Instruments) (74, 76), which was
844 equipped with a mode-locked Ti:Sapphire laser (MaiTai-HP
845 DeepSee, Newport Spectra-Physics) tuned to 927 nm, two
846 fluorescence detection channels for OGB-1 (HQ 510/84,
847 AHF/Chroma) and SR101 (HQ 630/60, AHF), and a wa-
848 ter immersion objective (CF175 LWD $\times 16/0.8\text{W}$, DIC N2,
849 Nikon, Germany). Image acquisition was performed with
850 custom-made software (ScanM by M. Müller and T.E.) run-
851 ning under IGOR Pro 6.3 for Windows (WaveMetrics), tak-
852 ing time-lapsed 64×64 pixel image scans ($\approx 100\text{ }\mu\text{m}$)²
853 at 7.8125 Hz (Figure 1c). For simplicity, we refer to such
854 a time-lapsed scan of a local population of GCL cells as

860 a “recording”. Despite the low frame rate, the Ca^{2+} re-
861 sponses can be related to the spike rate (77–80). For doc-
862umenting the position of the recording fields, the retina under
863 the microscope was oriented such that the most ventral
864 edge pointed always towards the experimenter. In addition,
865 higher resolution images (512×512 pixel) were acquired
866 and recording field positions relative to the optic nerve were
867 routinely logged.

868 **Data preprocessing.** Ca^{2+} traces were extracted for in-
869 dividual ROIs as described previously (6, 20). Extracted
870 traces \mathbf{c}_{raw} were then detrended to remove slow drifts in the
871 recorded signal that were unrelated to changes in the neural
872 response. First, a smoothed version of the traces, $\mathbf{c}_{\text{smooth}}$,
873 was calculated by applying a Savitzky-Golay filter of 3rd
874 polynomial order and a window length of 60 s using the
875 SciPy implementation `scipy.signal.savgol_filter`. This smoothed version was then subtracted from the
876 raw traces to yield the detrended traces.

$$\mathbf{c}_{\text{detrend}} = \mathbf{c}_{\text{raw}} - \mathbf{c}_{\text{smooth}}$$

877 To make traces non-negative (\mathbf{c}_+), we then clipped all
878 values smaller than the 2.5th percentile, $\eta_{2.5}$, to that value,
879 and then subtracted $\eta_{2.5}$ from the detrended traces:

$$\mathbf{c}_+ = \mathbf{c}_{\text{detrend}} - \eta_{2.5}$$

880 This procedure (i.e. clipping to, and subtracting $\eta_{2.5}$) was
881 more robust than simply subtracting the minimum.

882 Finally, traces were then divided by the standard devi-
883 ation within the time window before stimulus start at t_0 :

$$\mathbf{c} := \mathbf{c}_{\text{final}} = \frac{\mathbf{c}_{\text{nn}}}{SD(\mathbf{c}_{+[:t_0]})}$$

884 For training the model on movie response, we then es-
885 timated firing rates \mathbf{r} from the detrended Ca^{2+} traces \mathbf{c} using
886 the package C2S (<https://github.com/lucastheis/c2s>, Theis
887 et al. (80)).

888 **Inclusion criteria.** We applied a sequence of quality filter-
889 ing steps to recorded cells before analysis illustrated in Fig-
890 ure 1-figure supplement 1c. As a first step, we applied a
891 general response quality criterion, defined as a sufficiently
892 reliable response to the Moving bar stimulus (as quantified
893 by a quality index $QI_{MB} > 0.6$), or a sufficiently reliable
894 response to the chirp stimulus (as quantified by a quality
895 index $QI_{chirp} > 0.35$). The quality index is defined as in
896 ref.(6):

$$QI = \frac{\text{Var}[\langle \mathbf{r} \rangle_i]_t}{\langle \text{Var}[\mathbf{r}]_t \rangle_i}$$

897 where \mathbf{r} is the T by I response matrix (time samples
898 by stimulus repetitions) and $\langle \rangle_x$ and $\text{Var}[\cdot]_x$ denote the mean
899 and variance across the indicated dimension x , respectively.

900 The second and third step made sure only cells were
901 included that were assigned to a ganglion cell group (i.e.,
902 group index between 1 and 32) with sufficient confidence.

904 Confidence is defined as the probability assigned to the pre-
905 dicted class by the random forest classifier (see (81)), and
906 the threshold was set at ≥ 0.25 .

907 The fourth step made sure only cells with a sufficient
908 model prediction performance, defined as an average single-
909 trial test set correlation of $\langle C(\hat{r}^{(n)}, r_i^{(n)}) \rangle_i > .3$, were in-
910 cluded.

911 All cells passing steps 1-3 were included in the horizon
912 detection analysis (Figure 7); all cells passing steps 1-4 were
913 included in the MEI analysis (Figure 3); the "red" cells pass-
914 ing steps 1-4 were included in the MEI validation analysis
915 (Figure 4). In the process of analysing MEIs, we fitted DoGs
916 to their green and UV spatial component (see Methods sec-
917 tion Concentric anisotropic 2D Difference-of-Gaussians fit).
918 For the analysis of MEI properties (temporal frequency, cen-
919 tre size, chromatic contrast), we only included cells with a
920 sufficient DoG goodness-of-fit, determined as a value of the
921 cost function of $< .11$ for both green and UV on the re-
922 sulting DoG fit. This threshold was determined by visual
923 inspection of the DoG fits and led to the inclusion of 1613
924 out of 1947 RGCs in the MEI property analysis.

925 **Visual stimulation.** For light stimulation (imaging ex-
926 periments), we projected the image generated by a digi-
927 tal light processing (DLP) projector (lightcrafter DPM-
928 FE4500MKIIF, EKB Technologies Ltd) through the objec-
929 tive onto the tissue. The lightcrafter featured a light-guide
930 port to couple in external, band-pass filtered UV and green
931 LEDs (light-emitting diodes) (green: 576 BP 10, F37-576;
932 UV: 387 BP 11, F39-387; both AHF/Chroma) (82). To
933 optimise spectral separation of mouse M- and S-opsins,
934 LEDs were band-pass filtered (390/576 dual-band, F59-003,
935 AHF/Chroma). LEDs were synchronised with the micro-
936 scope's scan retrace. Stimulator intensity (as photoisomer-
937 ization rate, $10^3 P^* s^{-1}$ per cone) was calibrated to range
938 from ≈ 0.5 (black image) to ≈ 20 for M- and S-opsins, re-
939 spectively. Additionally, we estimated a steady illumina-
940 tion component of $\approx 10^4 P^* s^{-1}$ per cone to be present dur-
941 ing the recordings because of two photon excitation of pho-
942 topigments (74, 76). Before data acquisition, the retina was
943 adapted to the light stimulation by presenting a binary noise
944 stimulus (20×15 matrix, $(40 \mu\text{m})^2$ pixels, balanced random
945 sequence) at 5 Hz for 5 min to the tissue.

946 For electrophysiology experiments, stimuli were pre-
947 sented using a digital projector (DPM-FE4500MKII, EKB
948 Technologies Ltd) at a frame rate of 60 Hz and a spa-
949 tial resolution of 1140×912 pixels ($1.3 \mu\text{m}$ per pixel)
950 focused on the photoreceptor layer. Neutral density fil-
951 ters (Thorlabs), a triple-band pass filter (405 BP 20,
952 485 BP 20, 552 BP 16; 69000x, Chroma), and a cus-
953 tom LED controller circuit were used to attenuate the
954 light intensity of stimuli either to match that of the Ca^{2+}
955 imaging experiments (for MEI presentation) or to range
956 from $\approx 0\text{--}200 P^* s^{-1}$ per rod (for cell identification).
957 Stimuli were presented using Symphony software (<https://symphony-das.github.io/>) with custom extensions (<https://github.com/Schwartz-AlaLaurila-Labs/sa-labs-extension>).

960 **Identifying retinal ganglion cell types.** To functionally
961 identify RGC groups in the Ca^{2+} imaging experiments, we
962 used our default "fingerprinting" stimuli, as described ear-
963 lier (6). These stimuli included a full-field ($700 \mu\text{m}$ in diam-
964 eter) chirp stimulus, and a $300 \times 1,000 \mu\text{m}$ bright bar mov-
965 ing at $1,000 \mu\text{m} \cdot s^{-1}$ in eight directions across the recording
966 field (with the shorter edge leading; Figure 1b).

967 The procedure and rationale for identifying cells in
968 the electrophysiological recordings is presented in ref. (8).
969 Cells with responses that qualitatively matched that of the
970 OND and ON α types were included in the study. Fol-
971 lowing recording, cells were filled with AlexaFluor-488
972 by patch pipette and imaged under a two-photon micro-
973 scope. Dendrites were traced in Fiji (NIH) using the SNT
974 plugin (83). Dendritic arbours were computationally flat-
975 tened using a custom MATLAB tool (<https://doi.org/10.5281/zenodo.6578530>) based on the method in ref. (84) to
976 further confirm their identity as morphological type 73 from
977 ref. (9).

979 **Mouse natural movies.** The natural movie stimulus con-
980 sisted of clips of natural scenes recording outside in the
981 field with a specialised, calibrated camera (5). This cam-
982 era featured a fish-eye lens, and two spectral channels,
983 UV (band-pass filter F37-424, AHF, $> 90\%$ transmission
984 at $350\text{--}419 \text{ nm}$) and green (F47-510, $> 90\%$, $470\text{--}550 \text{ nm}$,
985 AHF), approximating the spectral sensitivities of mouse
986 opsins (35). In mice, eye movements often serve to sta-
987 bilise the image on the retina during head movements (48).
988 Therefore, the camera was also stabilised by mounting it on
989 a gimbal. As a result, the horizon bisected the camera's vi-
990 sual field.

991 A *mouse cam movie* frame contained a circular field
992 of view (FOV) of 180° corresponding to 437 pixels along
993 the diameter. To minimise the influence of potential chro-
994 matic and spatial aberrations introduced by the lenses, we
995 focused on image cut-outs (crops; $30^\circ \times 26^\circ$, equivalent to
996 72×64 pixels in size) from upper and lower visual field,
997 centred at $[28^\circ, 56^\circ]$ and $[-42^\circ, -31^\circ]$, respectively, rela-
998 tive to the horizon (for details, see (5)). Our *stimulus movie*
999 consisted of 113 movie clips, each 150 frames ($= 5 \text{ s}$) long.
1000 108 clips were randomly reordered for each recording and
1001 split into two 54 clips-long *training sequences*. The remain-
1002 ing 5 clips formed a fixed *test sequence* that was presented
1003 before, in between, and after the training sequences (Fig-
1004 ure 1b). To keep intensity changes at clip transitions small,
1005 we only used clips with mean intensities between 0.04 and
1006 0.22 (for intensities in $[0, 1]$). For display during the exper-
1007 iments, intensities were then mapped to the range covered by
1008 the stimulator, i.e. $[0, 255]$.

1009 **Convolutional neural network model of the retina.** We
1010 trained a convolutional neural network (CNN) model to pre-
1011 dict responses of RGCs to a dichromatic natural movie. The
1012 CNN model consisted of two modules, a convolutional core
1013 that was shared between all neurons, and a readout that was
1014 specific for each neuron (85).

1015 The core module was modelled as a two-layer convolutional neural network with 16 feature channels in each layer. 1016 Both layers consisted of space-time separable 3D convolutional kernels followed by a batch normalisation layer and 1017 an ELU (exponential linear unit) nonlinearity. In the first 1018 layer, sixteen $2 \times 11 \times 11 \times 21$ ($c=\#$ input channels (green 1019 and UV) $\times h=\text{height} \times w=\text{width} \times t=\#$ frames) kernels were 1020 applied as valid convolution; in the second layer, sixteen 1021 $16 \times 5 \times 5 \times 11$ kernels were applied with zero padding 1022 along the spatial dimensions. We parameterised the 1023 temporal kernels as Fourier series and added one time stretching 1024 parameter per recording to account for inter-experimental 1025 variability affecting the speed of retinal processing. More 1026 precisely, every temporal kernel was represented by the first 1027 k sine and cosine functions, with trainable weights and 1028 phases, on an evenly spaced temporal grid, where $k = 7$ for 1029 the first layer, and $k = 3$ for the second layer. Additionally, 1030 we introduced a trainable stretch parameter for every 1031 recording to account for faster and slower response kernels. 1032 For example, the first layer temporal kernels are 21 steps 1033 long. Then, in order to stay well under the Nyquist limit, 1034 we parameterise the kernels with $k = 21/3 = 7$ sines and 1035 cosines.

1036 For each of those sines and cosines a weight (α, β) is 1037 learned to represent the shape of the temporal responses 1038 kernel (shared among cells within a recording). Per scan i , the 1039 time grid t (21 steps from 0 to 1) is stretched by a factor τ_i to 1040 account for different response speeds. To avoid adding 1041 additional cycles (e.g., for stretch factors $\tau > 1$) this is masked 1042 by an exponential envelope

$$\epsilon(\tau) = \frac{1}{1 + \exp(-(t + \frac{21.0.95}{\tau}))} \quad (1)$$

1043 Thus,

$$w_i = \sum_j \alpha_j \sin(2\pi \cdot \tau_i \cdot t \cdot \epsilon(\tau_i)) + \beta_j \cos(2\pi \cdot \tau_i \cdot t \cdot \epsilon(\tau_i)). \quad (2)$$

1044 is the temporal kernel parameterisation, that allows the 1045 model to learn a shared temporal filter that is made faster 1046 or slower for each specific scan (86).

1047 In the readout, we modelled each cell's spatial receptive 1048 field (RF) as a 2D isotropic Gaussian, parameterised as 1049 $\mathcal{N}(\mu_x, \mu_y; \sigma)$. We then modelled the neural response as 1050 an affine function of the core feature maps weighted by the 1051 spatial RF, followed by a softplus nonlinearity.

1052 For the linearised version of the model, the architecture 1053 was exactly the same except for the fact that there was 1054 no ELU nonlinearity after both convolutional layers. The 1055 resulting CNN was therefore equivalent to an LN model.

1056 **Model training and evaluation.** We trained our network 1057 by minimising the Poisson loss

$$\sum_{n=1}^N \left(\hat{r}^{(n)} - r^{(n)} \log \hat{r}^{(n)} \right)$$

1058 where N is the number of neurons, $r^{(n)}$ is the measured 1059 and $\hat{r}^{(n)}$ the predicted firing rate of neuron n for an 1060 input of duration $t=50$ frames. We followed the training 1061 schedule of Lurz et al. (87). Specifically, we used early 1062 stopping (88) on the correlation between predicted and measured 1063 neuronal responses on the validation set, which consisted of 1064 15 out of the 108 movie clips. If the correlation failed to 1065 increase during any 5 consecutive passes through the entire 1066 training set (epochs), we stopped the training and restored 1067 the model to the best performing model over the course of 1068 training. We went through 4 cycles of early stopping, restoring 1069 the model to the best performing, and continuing training, 1070 each time reducing the initial learning rate of 0.01 by a 1071 learning rate decay factor of 0.3. Network parameters were 1072 iteratively optimised via stochastic gradient descent using 1073 the Adam optimiser (89) with a batch size of 32 and a chunk 1074 size (number of frames for each element in the batch) of 50. 1075 For all analyses and MEI generation, we used an ensemble 1076 of models as described in ref. (34). Briefly, we trained 5 1077 instances of the same model initialised with different random 1078 seeds. Inputs to the ensemble model were passed to each 1079 member and the final ensemble model prediction was obtained 1080 by averaging the outputs of the 5 members. For ease 1081 of notation, we thus redefine $\hat{r}^{(n)}$ to be the *ensemble* model 1082 prediction.

1083 After training, we evaluated model performance for 1084 each modelled neuron n as the correlation to the mean, i.e. 1085 the correlation between predicted response $\hat{r}^{(n)}$ and measured 1086 response $r^{(n)}$ to the held-out test sequence, the latter 1087 averaged across 3 repetitions $i = \{1, 2, 3\}$: $C(\hat{r}^{(n)}, \langle r_i^{(n)} \rangle_i)$. 1088 Unlike the single-trial correlation $C(\hat{r}^{(n)}, r_i^{(n)})$ which is 1089 always limited to values < 1 by inherent neuronal noise, a 1090 perfect model can in theory achieve a value of 1 for the 1091 correlation to the mean, in the limit of infinitely many repetitions 1092 when the sample average $\langle r^{(n)}_i \rangle_i$ is a perfect estimate of the 1093 true underlying response $\rho^{(n)}$. The observed correlation to 1094 the mean can thus be interpreted as an estimate of the 1095 fraction of the maximally achievable correlation achieved by our 1096 model. For deciding which cells to exclude from analysis, 1097 we used average single-trial correlation $(C(\hat{r}^{(n)}, r_i^{(n)}))_i$ 1098 since this measure reflects both model performance as well 1099 as reliability of the neuronal response to the movie stimulus 1100 for neuron n (see also Methods section on Inclusion criteria).

1101 **Synthesising MEIs.** We synthesised maximally exciting 1102 inputs for RGCs as described previously (32). Formally, for 1103 each model neuron n we wanted to find

$$\mathbf{x}^{*(n)} = \arg \max_{\mathbf{x}} \langle \hat{r}^{(n)}(\mathbf{x})_{30:50} \rangle_t, \quad (3)$$

1104 i.e. the input $\mathbf{x}^{*(n)}$ where the model neuron's response 1105 $\langle \hat{r}(\mathbf{x})_{30:50} \rangle_t$, averaged across frames 30 to 50, attains 1106 a maximum, subject to norm and range constraints 1107 (see below). To this end, we randomly initialised an input 1108 $\mathbf{x}_0^{(n)} \in \mathcal{R}^{c \times w \times h \times t}$ of duration $t=50$ frames with Gaussian 1109 1110 1111

1112 white noise, and then iteratively updated $x_i^{(n)}$ according to
1113 the gradient of the model neuron's response:

$$x_{i+1}^{(n)} = x_i^{(n)} + \lambda \frac{\delta}{\delta x_i^{(n)}} \langle \hat{r}^{(n)}(x_i^{(n)})_{30:50} \rangle_t, \quad (4)$$

1114 where $\lambda = 10$ was the learning rate. The optimisation was
1115 performed using Stochastic Gradient Descent (SGD), and
1116 was subject to a norm and a range constraint. The norm
1117 constraint was applied jointly across both channels and ensured
1118 that the L2 norm of each MEI did not exceed a fixed budget
1119 b of 30. The norm-constrained MEI $\tilde{x}_i^{(n)}$ was calculated at
1120 each iteration as

$$\tilde{x}_i^{(n)} = \frac{b}{\|x_i^{(n)}\|_2} \times x_i^{(n)} \quad (5)$$

1121 The range constraint was defined and applied for each
1122 colour channel separately and ensured that the range of the
1123 MEI values stayed within the range covered by the training
1124 movie. This was achieved by clipping values of the MEI ex-
1125 ceeding the range covered by the training movie to the min-
1126 imum or maximum value. Optimisation was run for at least
1127 100 iterations, and then stopped when the number of itera-
1128 tions reached 1,000, or when it had converged (whichever
1129 occurred first). Convergence was defined as 10 consecutive
1130 iterations with a change in model neuron activation of less
1131 than 0.001; model neuron activations ranged from ≈ 1 to \approx
1132 10. We denote the resulting MEI for neuron n as $x^{*(n)}$.

1133 **Analysing MEIs.** We analysed MEIs to quantify their spa-
1134 tial, temporal, and chromatic properties.

1135 **Spatial and temporal components of MEIs.** For each colour
1136 channel c , we decomposed the spatiotemporal MEIs into a
1137 spatial component and a temporal component by singular
1138 value decomposition:

$$U, S, V = \text{svd}(x_c^{*(n)})$$

1139 with $x_c^{*(n)} \in \mathcal{R}^{50 \times 288}$ for $c \in [\text{green, UV}]$ is the
1140 MEI of neuron n in a given colour channel with its spatial
1141 dimension ($18 \times 16 = 288$) flattened out. As a result, any
1142 spatiotemporal dependencies are removed and we only
1143 analyse spatial and temporal properties separately. The
1144 following procedures were carried out in the same manner
1145 for the green and the UV component of the MEI, and we
1146 drop the colour channel index c for ease of notation. The
1147 temporal component is then defined as the first left singular
1148 vector, $U_{:1}$, and the spatial component is defined as the
1149 first right singular vector, $V_{:1}^T$, reshaped to the original
1150 dimensions 18×16 .

1156 with soft-L1 loss function (40). The DoGs were parameter-
1157 ized by a location (μ_x, μ_y) shared between centre and sur-
1158 round, amplitudes A^c, A^s , variances $(\sigma_x^c, \sigma_y^c), (\sigma_x^s, \sigma_y^s)$, and
1159 rotation angles θ^c, θ^s separately for centre and surround:

$$\text{DoG} = G^c - G^s$$

1160 with

$$G^c(x, y) = A^c \exp(-f^c(x - \mu_x)^2 - 2g^c(y - \mu_y)(x - \mu_x) + h^c(y - \mu_y)^2)$$

1161 and

$$f^c = \frac{\cos^2 \theta^c}{2\sigma_x^c} + \frac{\sin^2 \theta^c}{2\sigma_y^c},$$

$$g^c = \frac{\sin 2\theta^c}{4\sigma_y^c} - \frac{\sin 2\theta^c}{4\sigma_y^c},$$

$$h^c = \frac{\sin^2 \theta^c}{2\sigma_x^c} + \frac{\cos^2 \theta^c}{2\sigma_y^c},$$

1162 and likewise for G^s . We initialised (μ_x, μ_y) in the fol-
1163 lowing way: Since we set the model readout's location pa-
1164 rameters to $(0, 0)$ for all model neurons when generating
1165 their MEIs, we also expected the MEIs to be centred at $(0,$
1166 $0)$, as well. Hence, we determined the location of the min-
1167 imum and the maximum value of the MEI; whichever was
1168 closer to the centre $(0,0)$ provided the initial values for the
1169 parameters (μ_x, μ_y) . Starting from there, we then first fit a
1170 single Gaussian to the MEI, and took the resulting pa-
1171 rameters as initial parameters for the DoG fit. This was a con-
1172 strained optimisation problem, with lower and upper bounds
1173 on all parameters; in particular, such that the location pa-
1174 rameter would not exceed the canvas of the MEI, and such that
1175 the variance would be strictly positive.

1176 **MEI properties.**

1177 **Centre size** We defined the diameter of the centre of
1178 the MEI in the horizontal and the vertical orientation,
1179 respectively, as $d_x^c = 2\sigma_x^c$ and $d_y^c = 2\sigma_y^c$. The centre size
1180 was calculated as $\frac{1}{2}(d_x^c + d_y^c)$. We then estimated a contour
1181 outlining the MEI centre as the line that is defined by all
1182 points at which the 2D centre Gaussian G^c attains the value
1183 $G^c(x, y)$ with $(x, y) = (\mu_x + \sigma_x^c, \mu_y + \sigma_y^c)$. The centre mask
1184 m was then defined as a binary matrix with all pixels within
1185 the convex hull of this contour being 1 and all other pixels
1186 set to 0. This mask is used for calculating centre chromatic
1187 contrast (see below).

1188 **Temporal frequency** To estimate temporal frequency of
1189 the MEIs, we estimated the power spectrum of the temporal
1190 components using a Fast Fourier Transform after attenuating
1191 high frequency noise by filtering with a 5th order low-pass

1152 **Concentric anisotropic 2D Difference-of-Gaussians fit.** We
1153 modelled the spatial component as concentric anisotropic
1154 Difference-of-Gaussians (DoG) using the nonlinear least-
1155 squares solver `scipy.optimize.least_squares`

1193 Butterworth filter with cutoff frequency 10 Hz. We then es-
 1194 timated the mean frequency of the temporal component by
 1195 calculating an average of the frequency components, each
 1196 weighted with its relative power.

1197 **Contrast** The contrast of the MEIs in the two channels,
 1198 $\gamma(\mathbf{x}_c^{*(n)})$ for $c \in [\text{green, UV}]$, was defined as the difference
 1199 between the mean value within the centre mask m at the two
 1200 last peaks of the temporal component of the MEI in the UV
 1201 channel at time points t_2 and t_1 :

$$\gamma(\mathbf{x}_c^{*(n)}) = (\mathbf{x}_c^{*(n)} \odot m)(t_2) - (\mathbf{x}_c^{*(n)} \odot m)(t_1),$$

1202 where \odot denotes the element-wise multiplication of the
 1203 MEI and the binary mask. (see Figure 3f). The peaks were
 1204 found with the function `scipy.signal.find_peaks`,
 1205 and the peaks found for the UV channel were used to calcu-
 1206 late contrast both in the green and the UV channel.

1207 Validating MEIs experimentally.

1208 **Generating MEI stimuli.** To test experimentally whether the
 1209 model correctly predicts which stimuli would maximally ex-
 1210 cite RGCs of different RGC groups, we performed a new set
 1211 of experiments (numbers indicated in red in Figure 1-figure
 1212 supplement 1Ic), where we complemented our stimulus set
 1213 with MEI stimuli. For the MEI stimuli, we selected 11
 1214 RGCs, chosen to span the responses space and to represent
 1215 both well-described and poorly understood RGC groups, for
 1216 which we generated MEIs at different positions on a 5×5
 1217 grid (spanning $110\mu\text{m}$ in vertical and horizontal direction).
 1218 We decomposed the MEIs as described above, and recon-
 1219 structed MEIs as rank 1 tensors by taking the outer product
 1220 of the spatial and temporal components:

$$\bar{\mathbf{x}}^* = S_{11} U_{:,1} \otimes V_{:,1}^T$$

1221 The MEI stimuli, lasting 50 frames (1.66 s) were
 1222 padded with 10 frames (.34 s) of inter-stimulus grey, and
 1223 were randomly interleaved. With 11 stimuli, presented at
 1224 25 positions and lasting 2 s each, the total stimulus duration
 1225 was $11 \times 25 \times 2 \text{ s} = 550 \text{ s}$. Since the model operated on a
 1226 z-scored (0 mean, 1 SD) version of the movie, MEIs as pre-
 1227 dicted by the model lived in the same space and had to be
 1228 transformed back to the stimulator range ([0, 255]) before
 1229 being used as stimuli in an experiment by scaling with the
 1230 movie's SD and adding the movie's mean. The MEIs' green
 1231 channel was then displayed with the green LED, and the UV
 1232 channel was displayed with the UV LED. For experiments at
 1233 Northwestern University, an additional transform was nec-
 1234 essary to achieve the same levels of photoreceptor activation
 1235 (photoisomerization rates) for M- and S-cones with different
 1236 LEDs. To ensure proper chromatic scaling between the dif-
 1237 ferent experimental apparatuses with different spectral pro-
 1238 files, we described the relative activation of M- and S-cones
 1239 by the green and UV LEDs in the stimulation setup used in
 1240 the two photon imaging experiments (setup A) by a matrix

$$\mathbf{A} = \begin{bmatrix} a_{mg} & a_{sg} \\ a_{mu} & a_{su} \end{bmatrix} = \begin{bmatrix} 1 & 0.19 \\ 0 & 1 \end{bmatrix},$$

1241 and the relative activation of M- and S-cones by
 1242 the stimulation setup used in the patch-clamp experiments
 1243 (setup B) by a matrix

$$\mathbf{B} = \begin{bmatrix} b_{mg} & b_{sg} \\ b_{mu} & b_{su} \end{bmatrix} = \begin{bmatrix} 1 & 0.9 \\ 0.035 & 1 \end{bmatrix},$$

1244 where diagonal entries describe the activation of M-
 1245 cones by the green LED, and of S-cones by the UV LED,
 1246 and entries in the off-diagonal describe the cross-activation
 1247 (i.e., M-cones by UV-LED and S-cones by green LED). The
 1248 activation of M-cones and S-cones $\mathbf{e}^T = (e_m, e_s)$ by a stim-
 1249 ulus $\mathbf{x} \in \mathcal{R}^{2 \times 1}$ displayed on a given stimulation setup was
 1250 approximated as $\mathbf{e} = \mathbf{A}\mathbf{x}$ (90). Hence, a stimulus \mathbf{x}' dis-
 1251 played on setup B, defined as $\mathbf{x}' = \mathbf{B}^{-1}\mathbf{A}\mathbf{x}$, will achieve
 1252 the same photoreceptor activation as stimulus \mathbf{x} displayed
 1253 on setup A. Since the solution exceeded the valid range of
 1254 the stimulator ([0, 255]), we added an offset and multiplied
 1255 with a scalar factor to ensure all stimuli were within the valid
 1256 range.

1257 **Analysing RGC responses to MEI stimuli.** We wanted to
 1258 evaluate the responses of RGCs to the MEI stimuli in a spa-
 1259 tially resolved fashion, i.e. weighting responses to MEIs
 1260 displayed at different locations proportional to the strength
 1261 of the RGCs RF at that location. In order to be able to
 1262 meaningfully compare MEI responses between RGCs and
 1263 across groups, for each RGC, we first centred and scaled
 1264 the responses to zero mean and a standard deviation of 1.
 1265 Then, for each RGC n , we computed a spatial average of its
 1266 responses, weighting its responses at each spatial location
 1267 (x, y) proportional to the Gaussian density $\mathcal{N}_{\mu_n, \sigma_n}(x, y)$,
 1268 where the parameters of the Gaussian $\mu_n = (\mu_x, \mu_y), \sigma_n$
 1269 were the model's estimated readout parameters for neuron
 1270 n (Figure 4b,c,d left):

$$\langle \mathbf{r}^{(n)} \rangle_{x,y} = \sum_{x'=1}^5 \sum_{y'=1}^5 \mathbf{r}_{x',y'}^{(n)} \cdot \mathcal{N}_{\mu_n, \sigma_n}(x', y')$$

1271 where $\mathbf{r}_{x',y'}^{(n)} \in \mathcal{R}^{11 \times 60}$ is the 60 frames (2 s) long re-
 1272 sponse of neuron n to an MEI at position $(x, y) = (x', y')$,
 1273 resampled from the recording frame rate of 7.81 Hz to
 1274 30 Hz. We then averaged $\langle \mathbf{r}^{(i)} \rangle_{x,y}$ across time in the op-
 1275 timisation time window, i.e. frames 30-50, to get a scalar
 1276 response $\tilde{r}^{(n)} = \langle \mathbf{r}^{(n)} \rangle_{x,y,t}$ for each MEI stimulus (Figure
 1277 4d).

1278 **Selectivity index.** To quantify the selectivity of the response
 1279 $\tilde{r}^{(n)}(\mathbf{x}_i^*)$ of an RGC n to an MEI \mathbf{x}_i^* , we defined a selec-
 1280 tivity index as follows. First, we standardised the responses
 1281 $\tilde{r}^{(n)}$ across all MEIs by subtracting the mean and dividing
 1282 by the standard deviation. The selectivity index of RGC
 1283 group G_g to MEI \mathbf{x}_i^* was then defined as

$$1284 \quad \text{SI}_g(\mathbf{x}_i^*) = \langle \tilde{r}^{(n)}(\mathbf{x}_i^*) - \frac{1}{10} \sum_{j=1}^{11} \delta_{ij} \tilde{r}^{(n)}(\mathbf{x}_j^*) \rangle_n,$$

1285 where δ_{ij} is the Kronecker delta. In words, the SI is the
 1286 difference (in units of SD response) between the response to
 1287 the MEI of interest (\mathbf{x}_i^*) and the mean response to all other
 1288 (10) MEIs, $\frac{1}{10} \sum_{j=1}^{11} \delta_{ij} \tilde{r}^{(n)}(\mathbf{x}_j^*)$, averaged across all cells
 1289 n belonging to the group of interest G_g .

1290 **Characterising nonlinear processing of chromatic
 1291 contrast space.** We wanted to analyse the tuning of
 1292 G_{28} /tSbC RGCs to chromatic contrast and to this end, we
 1293 mapped the model response and its gradient across chro-
 1294 matic contrast space (Figure 6). Specifically, the MEIs
 1295 have $d = 2 \times 18 \times 16 \times 50 = 28,800$ pixels and dimensions,
 1296 14,400 for each colour channel. Now let $x^{*(n)} \in \mathcal{R}^{1 \times 28800}$
 1297 be the cell's MEI estimated using the LN model, with the
 1298 first $d=14,400$ dimensions defining the green pixels and the
 1299 remaining dimensions defining the UV pixels. Then for each
 1300 cell we consider a two-dimensional subspace spanned by
 two basis vectors $\mathbf{e}_1, \mathbf{e}_2$ where

$$\mathbf{e}_1 = \begin{bmatrix} x_1^{*(n)} \\ x_2^{*(n)} \\ \vdots \\ x_d^{*(n)} \\ 0 \\ \vdots \\ 0 \end{bmatrix} \quad \mathbf{e}_2 = \begin{bmatrix} 0 \\ \vdots \\ 0 \\ x_1^{*(n)} \\ x_2^{*(n)} \\ \vdots \\ x_d^{*(n)} \end{bmatrix}$$

1301 In words, the basis vectors consist of the UV compo-
 1302 nent of the MEI in the UV channel and 0s in the green
 1303 channel for \mathbf{e}_1 , and of 0s in the UV channel and the UV
 1304 component of the MEI in the green channel for \mathbf{e}_2 . We chose
 1305 this subspace due to its vicinity to the optimum of the neu-
 1306 ron's tuning curve, and we chose the UV MEI as compo-
 1307 nent of both basis vectors, since the green and UV compo-
 1308 nent of G_{28} MEIs were very similar except for their tem-
 1309 poral contrast (see Figure 3-figure supplement 1II). We then
 1310 sampled 11 points along each dimension, equally spaced be-
 1311 tween $[-1, 1]$, which resulted in stimuli that are identical in
 1312 terms of their spatial and temporal properties and only differ
 1313 in their contrast. We then evaluated the model neuron re-
 1314 sponse at these points in the subspace (Figure 6d). We also
 1315 evaluated the gradient of the model neuron response at these
 1316 points and plotted the direction of the gradient projected into
 1317 the subspace spanned by $\mathbf{e}_1, \mathbf{e}_2$ (Figure 6b,c).

1318 **Detection performance analysis.** To test the per-
 1319 formance of individual RGCs of different groups in detecting
 1320 the target class of inter-clip transitions (ground-to-sky) from
 1321 all other classes of inter-clip transitions, we performed a
 1322 receiver operating characteristic (ROC) analysis (47). For
 1323 each RGC, we calculated its response to an inter-clip transi-
 1324 tion occurring at time t_0 as the baseline-subtracted aver-
 1325 age response within 1 second following the transition, i.e.

1326 $\frac{1}{T} \sum_{t=0}^T r(t) - r(t_0)$, with $T=30$ frames at 30 Hz. For all
 1327 $n=40$ equally spaced thresholds within the response range of
 1328 a RGC, we then calculated the true positive rate (TPR) and
 1329 false positive rate (FPR) of a hypothetical classifier classi-
 1330 fying all transitions eliciting an above-threshold response as
 1331 a positive, and all other transitions as negative. Plotting the
 1332 TPR as a function of FPR yields an ROC curve, the area
 1333 under which (AUC) is equivalent to the probability that the
 1334 RGC will respond more strongly to a randomly chosen inter-
 1335 clip transition of the target class than to a randomly chosen inter-clip
 1336 transition of a different class. The AUC thus is a
 1337 measure of performance for RGCs in this detection task.

1338 **Detection task in simulation.** We simulated the four types
 1339 of transitions (sky-sky, sky-ground, ground-ground, ground-
 1340 sky) in natural scenes to include various visual context
 1341 changes across velocities, which could be triggered by dif-
 1342 ferent behaviours such as locomotion or eye movements.
 1343 With the simulated context-changing stimuli, we predicted
 1344 model neuron responses *in-silico* and then determined if G_{28}
 1345 could perform the detection task robustly well across speeds.

1346 For generating the stimuli, 500 frames were randomly
 1347 extracted from the same mouse natural movies used for the
 1348 2P-imaging experiments. For each frame, we simulated vi-
 1349 sual transitions by moving a 72×64 pixel-large window
 1350 along a fixed trajectory (Figure 7h bottom) at four different
 1351 angular velocities: 50, 150, 250, and $350^\circ/\text{s}$, correspond-
 1352 ing to 4, 12, 20, and 28 pixels per frame, respectively (Figure 6-
 1353 figure supplement 3VIIIa,b). Each edge of the trajectory is
 1354 220 pixels long, covering 90.6° of visual angle. Each se-
 1355 lected scene frame was sampled 8 times (that is, twice per
 1356 velocity). To avoid potential biases due to asymmetries in
 1357 the mouse natural movie, we sampled each frame for each
 1358 velocity both in clockwise and counterclockwise direction.
 1359 The stimuli were then down-sampled to 18×14 pixels and
 1360 shown to the model at a frame rate of 30 Hz. Because the
 1361 trajectories contained different numbers of moving frames
 1362 for the 4 velocities, we “padded” the stimuli at the begin-
 1363 ning and the end of each transition stimulus by duplicating
 1364 the start and end frames, resulting in a total of 60 frames
 1365 each (see illustration in Figure 6-figure supplement 3VIIIb).

1366 Statistical analysis.

1367 **Permutation test.** We wanted to test how likely the differ-
 1368 ence in AUC observed for different RGC groups are to oc-
 1369 cur under the null hypothesis that the underlying distribu-
 1370 tions they are sampled from are equal. To this end, we per-
 1371 formed a permutation test. We generated a null distribution
 1372 for our test statistic, the absolute difference in AUC values
 1373 ΔAUC , by shuffling the RGC group labels of the two groups
 1374 of interest (e.g. G_{28} and G_{24}) and calculating the test statis-
 1375 tic with shuffled labels 100,000 times. We only included
 1376 RGC groups with at least $N=4$ cells in this analysis. We then
 1377 obtained a p-value for ΔAUC observed with true labels as
 1378 the proportion of entries in the null distribution larger than
 1379 ΔAUC .

1380 **Bootstrapped confidence intervals.** We bootstrapped con-
1381 fidence intervals for ΔAUC (Figure 7 and Figure 6-figure
1382 supplement 2VII). For ΔAUC , we generated a bootstrapped
1383 distribution by sampling 100 times with replacement from the
1384 AUC values of the two groups that were being com-
1385 pared and calculated ΔAUC . We then estimated the 95 %
1386 confidence interval for ΔAUC as the interval defined by the
1387 2.5th and 97.5th percentile of the bootstrapped distribution
1388 of ΔAUC .

1389 For $\Gamma(\phi_s, \phi_{\nu_g})$, we generated a bootstrapped distribution
1390 by sampling 100 times with replacement from the MEI
1391 responses of RGC group g and then calculating $\text{RDM}^{\phi_{\nu_g}}$
1392 and $\Gamma(\phi_s, \phi_{\nu_g})$ for each sample. We then estimated the 95
1393 % confidence interval for $\Gamma(\phi_s, \phi_{\nu_g})$ as the interval defined
1394 by the 2.5th and 97.5th percentile of the bootstrapped distribution
1395 of $\Gamma(\phi_s, \phi_{\nu_g})$.

1396 **Estimating effect size.** The effect size of difference in AUC
1397 observed for different RGC groups l and k , ΔAUC (Figure
1398 7 and Figure 6-figure supplement 2VII), was estimated
1399 as Cohen's d (91, 92):

$$\frac{|m_k - m_l|}{s},$$

1400 with

$$s = \sqrt{\frac{(N_k - 1)s_k^2 + (N_l - 1)s_l^2}{N_k + N_l - 2}}$$

1401 and m_k and s_k the sample mean and standard devia-
1402 tion, respectively, of the AUC observed for the N_k RGCs of
1403 group k .

1404 **Estimating linear correlation.** Wherever the linear corre-
1405 lation between two paired samples x and y of size N was
1406 calculated (for evaluating model performance, Figure 2, Figure
1407 1-figure supplement 1I, Figure 4-figure supplement 1IV,
1408 we used Pearson's correlation coefficient:

$$C_{xy} = \frac{\sum_i^N (x_i - \bar{x})(y_i - \bar{y})}{\sqrt{\sum_i^N (x_i - \bar{x})^2} \sqrt{\sum_i^N (y_i - \bar{y})^2}}$$

1409 Data availability

1410 The data and the movie stimulus will be made available at
1411 <https://retinal-functomics.net> upon journal publication.

1412 Code availability

1413 Custom analysis and model training code will be made
1414 available at <https://github.com/eulerlab> upon journal publi-
1415 cation.

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1781 **Supplementary information**

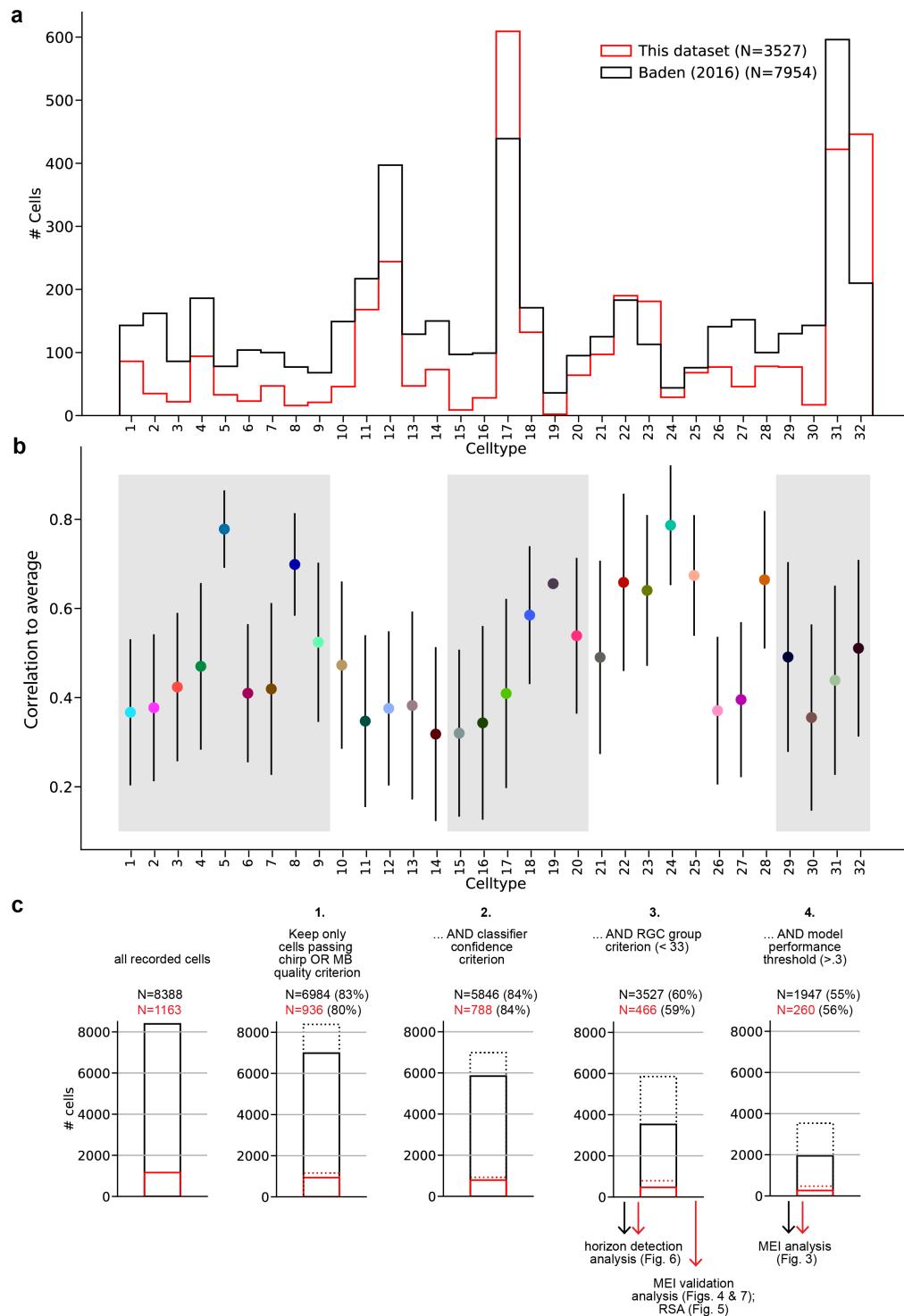


Figure 1-figure supplement 1. (a) Distribution across cell types for this dataset, and for the dataset described in Baden et al. (6) which was the basis for our classifier (81). (b) Mean \pm SD of model performance, evaluated as correlation between model prediction and RGC response on the 25 s long test sequence, averaged across 3 repetitions of the test sequence, for each cell type. (c) Response quality, RGC group assignment and model performance filtering pipeline showing the consecutive steps and the fraction of cells remaining after each step. Black bars and numbers indicate cells from all experiments (i.e. all RGCs for which we recorded chirp, MB, and movie responses), red bars and numbers indicate the subset of cells recorded in the MEI validation experiments (i.e. those RGCs for which we *additionally* recorded MEI stimuli responses). Dotted bars indicate the number of cells before the current filtering step. The filtering steps were as follows: 1. Keep only cells that pass the chirp OR MB quality criterion ($QI_{MB} > .6$ OR $QI_{chirp} > .35$). 2. Keep only cells that the classifier assigns to a group with confidence $\geq .25$. 3. Keep only cells assigned to a ganglion cell group (groups 1-32; groups 33-46 are amacrine cell groups). 4. Keep only cells with sufficiently high model performance ($\langle C(\hat{r}^{(n)}, r_i^{(n)}) \rangle_i > .3$). All cells passing steps 1-3 were included in the horizon detection analysis (Figure 7); all cells passing steps 1-4 were included in the MEI analysis (Figure 3); the “red” cells passing steps 1-4 were included in the MEI validation analysis (Figure 4). All quality criteria are described in the Methods section.



Figure II 3-figure supplement 1. Example MEIs for example cell types. Rows in each panel as in Figure 4a.

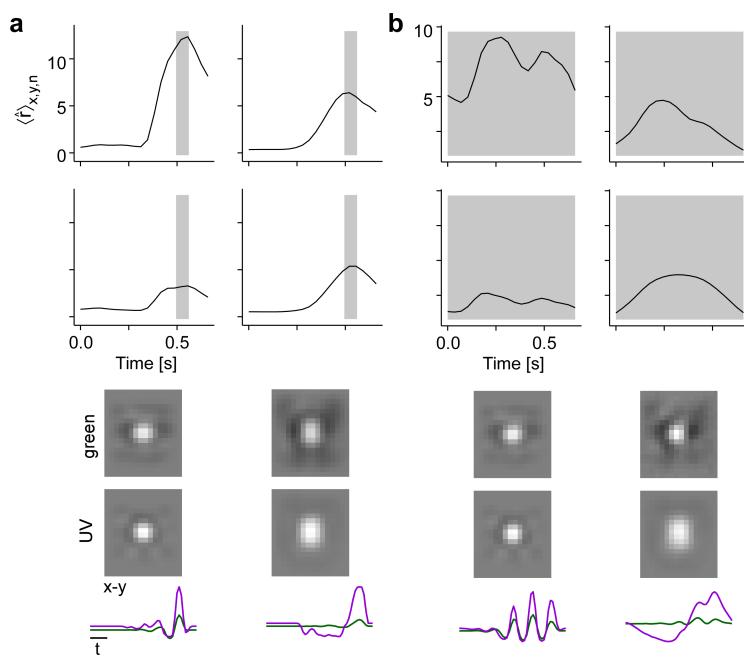


Figure III 3-figure supplement 2. Illustration of how different time windows for optimisation affect MEI temporal properties. **(a)** MEIs (bottom panels) and model neuron responses (top panels) for a short optimisation window of 2 frames ($\approx .066$ s, indicated by grey shaded area). The top row shows the responses of a more transient RGC to its own MEI (left stimulus) and to the MEI of a more sustained RGC (right stimulus). The bottom row shows the responses of the more sustained RGC to its own MEI (right stimulus) and to the MEI of the more transient RGC (right stimulus). **(b)** MEIs (bottom panels) and model neuron responses (top panels) for a longer optimisation window of 20 frames ($\approx .66$ s, indicated by grey shaded area) as used throughout the paper. The top row shows the responses of a more transient RGC to its own MEI (left stimulus) and to the MEI of a more sustained RGC (right stimulus). The bottom row shows the responses of the more sustained RGC to its own MEI (right stimulus) and to the MEI of the more transient RGC (right stimulus). Same cells as in (a).

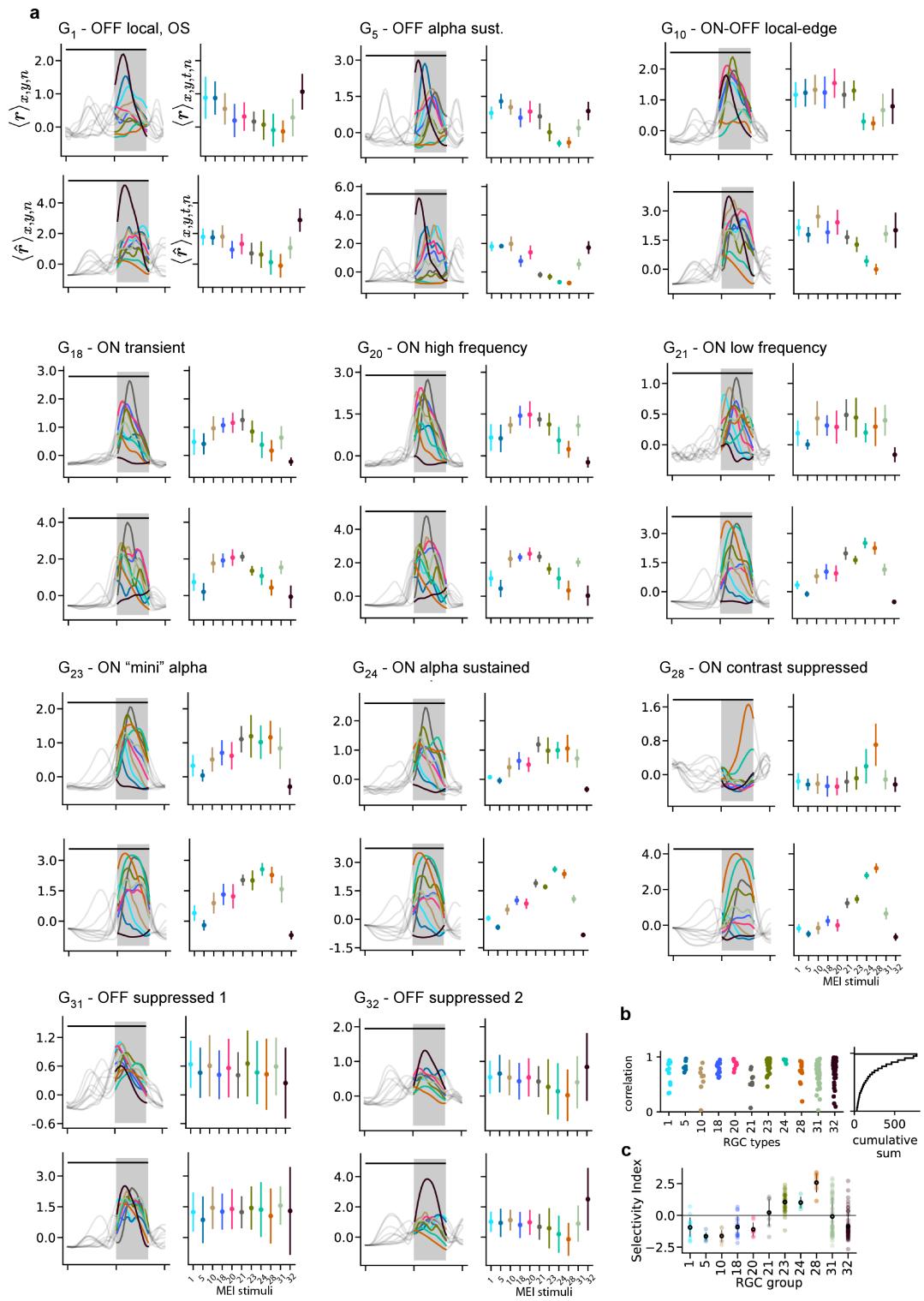


Figure IV 4-figure supplement 1. (a) Recorded (top, r) and predicted (bottom, \hat{r}) responses to the 11 different MEIs for all example cell types. Left: responses are averaged across the indicated dimensions x, y, n: different MEI locations (x, y) and RGCs in a group (n); black bar indicates stimulus duration (from 0 to 1.66 s), grey rectangle marks optimisation time window (from 1 to 1.66 s). Right: Responses to different MEIs, additionally averaged across time (t) within the optimisation time window. Error bars indicated SD across cells. (b) Correlation between the measured and predicted response magnitudes to the MEI stimuli per example cell type. Cumulative histogram is across all N=788 cells; 50% of cells have a correlation between measured and predicted response magnitude of ≥ 0.8 . (c) Mean \pm SD of selectivity index (see Methods) for the example cell groups, indicating the difference in response to MEI 28 vs. the average response to all other MEIs in units of standard deviation of the response.

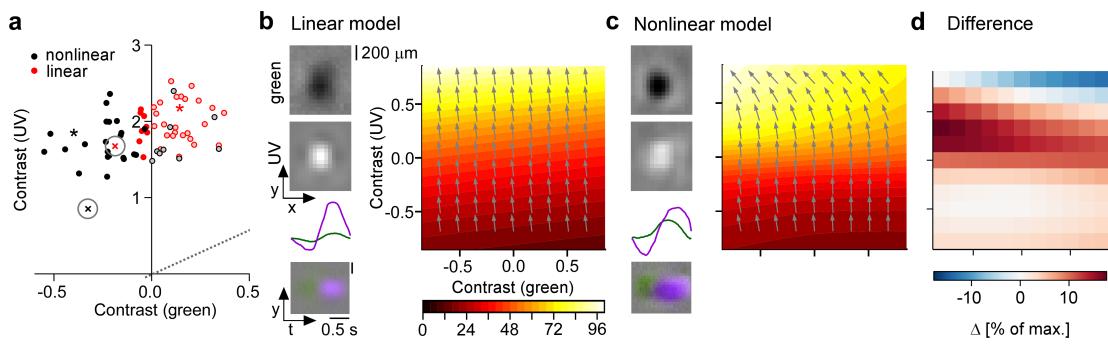


Figure V 5-figure supplement 1. (a) Distribution of green and UV MEI centre contrast for a linear-nonlinear (LN) model (red) and a CNN model (black); from Figure 6a. (b,c) Left: MEIs for a second example cell of RGC group G₂₈, generated with the LN model (b) or the CNN model (c). The cell's MEI centre contrast for both models is marked in (a) by cross. Right: Respective tuning maps of example neuron in chromatic contrast space. Colours represent responses in % of maximum response; arrows indicate the direction of the gradient across chromatic contrast space. (d) Difference in response between LN and CNN model (in % of maximum response).

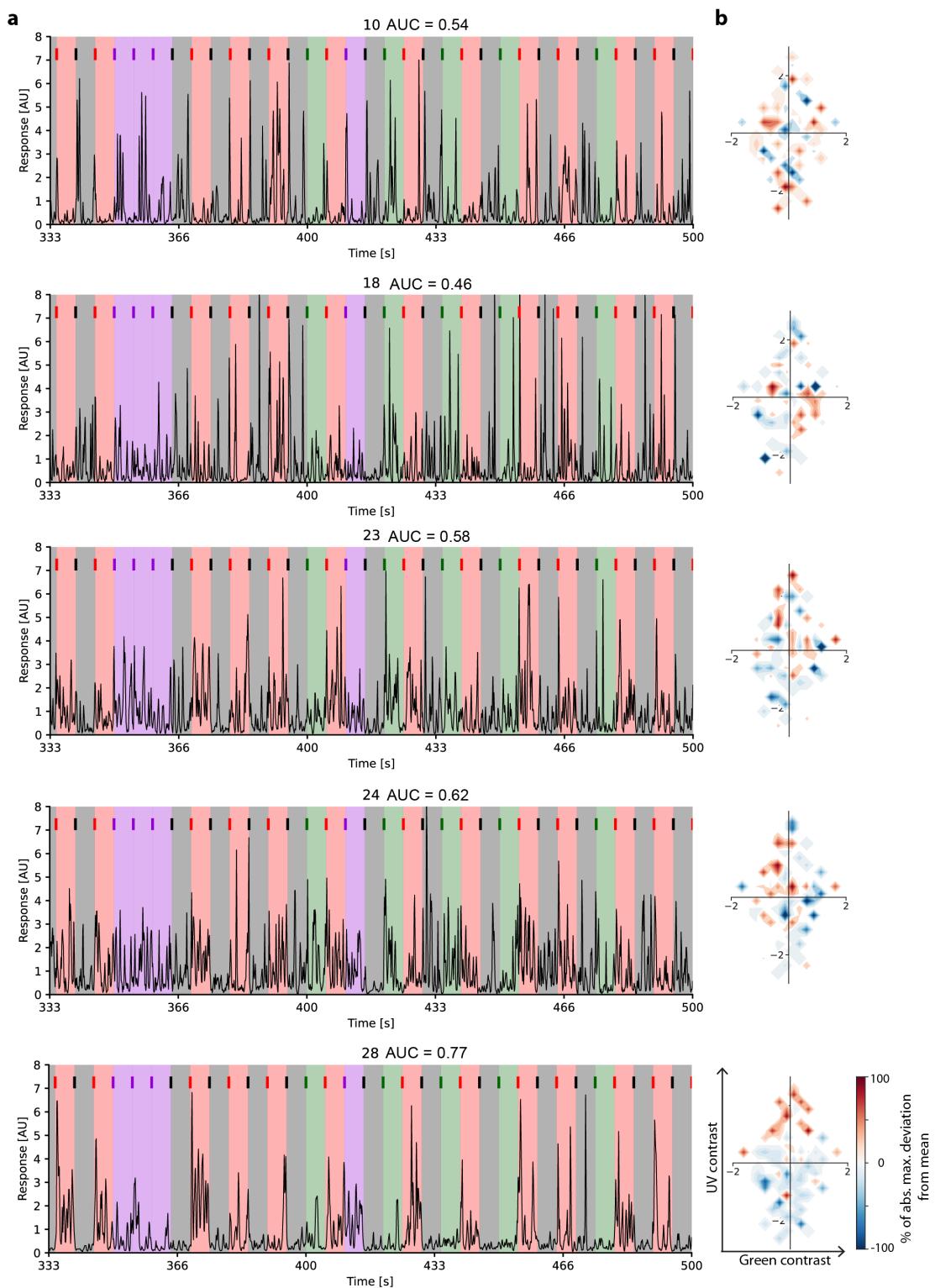


Figure VI 6-figure supplement 1. (a) Traces of example cells of different cell groups (G_{10} , G_{18} , G_{23} , G_{24} , G_{28}) from a single recording field, responding to 33 (of 122) inter-clip transitions. Inter-clip transitions are colour-coded by transition type (red: ground-to-sky, purple: sky-to-sky, green: ground-to-ground, black: sky-to-ground). (b) The resulting tuning maps in chromatic contrast space.

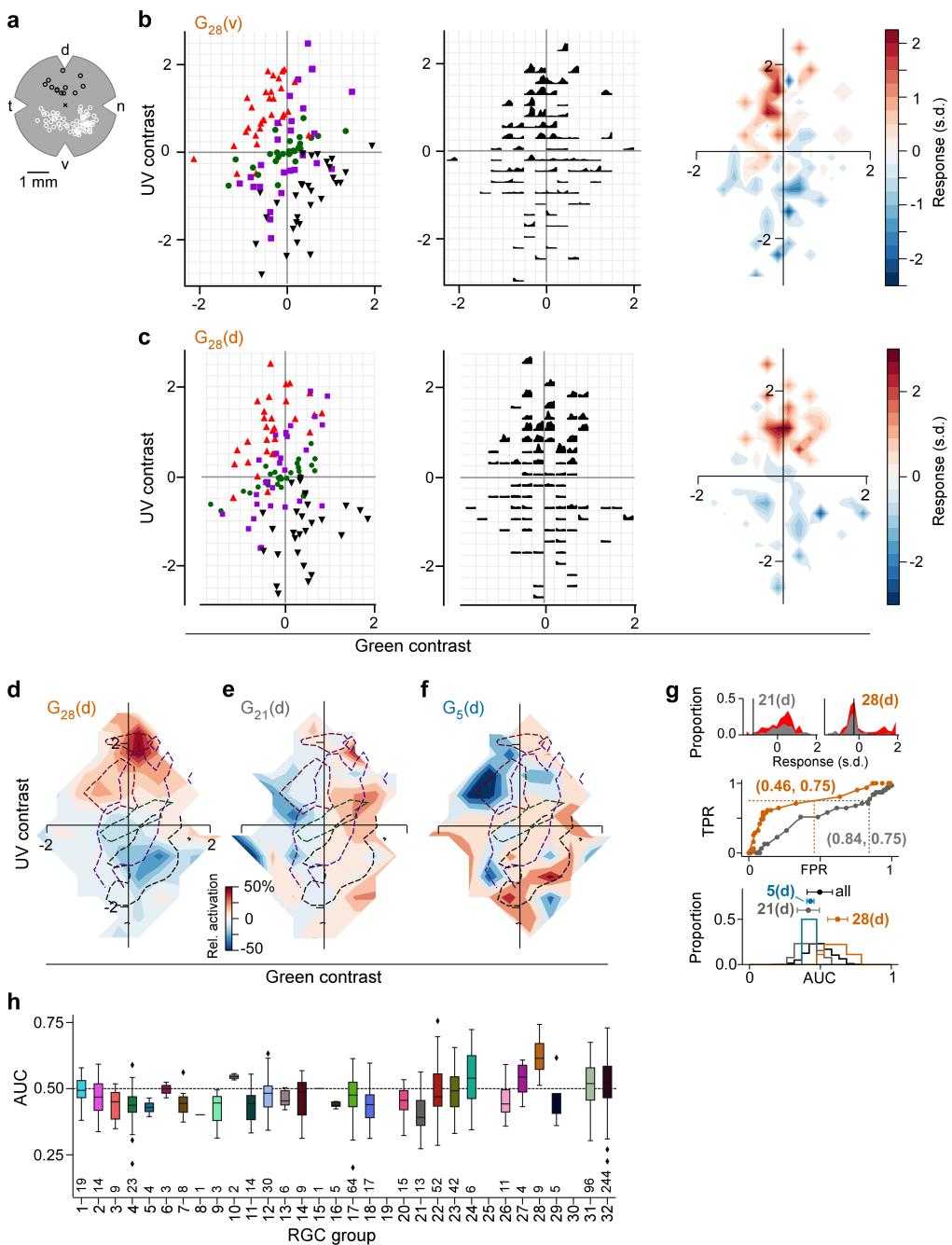


Figure VII 6-figure supplement 2. (a) Illustration of a flat-mounted retina, with recording fields in the dorsal (black circles) and ventral (white circles) retina (cross marks optic disc; d, dorsal; v, ventral; t, temporal; n, nasal). (b) *Left*: Distribution of green and UV contrasts of $N=122$ inter-clip transitions seen by a *ventral* group 28 (G_{28}) RGC, coloured by transition type (red triangle, ground-to-sky; green disk, ground-to-ground; black downward triangle, sky-to-ground; purple square, sky-to-sky). *Middle*: Responses of example RGC in the 1's following an inter-clip transition, averaged across transitions within the bins indicated by the grid. *Right*: Responses transformed into a tuning map by averaging within bins as defined by grid (*Left*). Responses are z-scored ($\mu = 0, \sigma = 1$). (c) Like (b) but for a *dorsal* G_{28} RGC. (d) Tuning map of $N=9$ *dorsal* G_{28} RGCs, created by averaging the tuning maps of the individual RGCs. (e) Same as (d) for $N=13$ G_{21} RGCs. (f) Same as (d) for $N=4$ G_5 RGCs. (g) *Top*: Illustration of ROC analysis for two dorsal RGCs, a G_{21} (left) and a G_{28} (right). For each RGC, responses were binned to all inter-clip transitions, separately for ground-to-sky (red) and all other transitions (grey). *Middle*: Sliding a threshold d across the response range, classifying all transitions with response $> d$ as ground-to-sky, and registering the false-positive-rate (FPR) and true-positive-rate (TPR) for each threshold yields an ROC curve (middle). Numbers in brackets indicate (FPR, TPR) at the threshold indicated by black vertical line in histogram plots. *Bottom*: We evaluated performance for each cell as the area under the ROC curve (AUC), and plotted the distribution across AUC values for all cells (black), for G_5 (blue), for G_{21} (grey), and for G_{28} (orange). Among the dorsal RGCs, G_{28} RGCs achieved the highest AUC on average (mean \pm SD AUC, G_{28} ($N=9$ cells)): 0.62 ± 0.07 ; all other groups ($N=720$): 0.49 ± 0.09 , $\Delta AUC = 0.13$, bootstrapped 95% confidence interval $CI_{95} = [0.08, 0.18]$, Cohen's $d = 1.45$, two-sample permutation test G_{28} vs. all other groups (see Methods): $p = 0$ with 100,000 permutations; next-best performing G_{24} ($N=6$): 0.54 ± 0.12 , $\Delta AUC = 0.08$, bootstrapped 95% confidence interval $CI_{95} = [0.01, 0.18]$, Cohen's $d = 0.87$; two-sided t -test G_{28} vs. G_{24} : $p = .15$ with 100,000 permutations (not significant). AUC mean \pm SD indicated as dots and horizontal lines above histograms. (h) Boxplot of AUC distributions per cell type (*dorsal*). The box extends from the first quartile (Q_1) to the third quartile (Q_3) of the data; the line within a box indicates the median. The whiskers extend to the most extreme points still within $[Q_1 - 1.5 \times IQR, Q_3 + 1.5 \times IQR]$, IQR = inter-quartile range. Diamonds indicate points outside this range. All elements of the plot (upper and lower boundaries of the box, median line, whiskers, diamonds) correspond to actual observations in the data. Numbers of RGCs for each type are indicated in the plot.

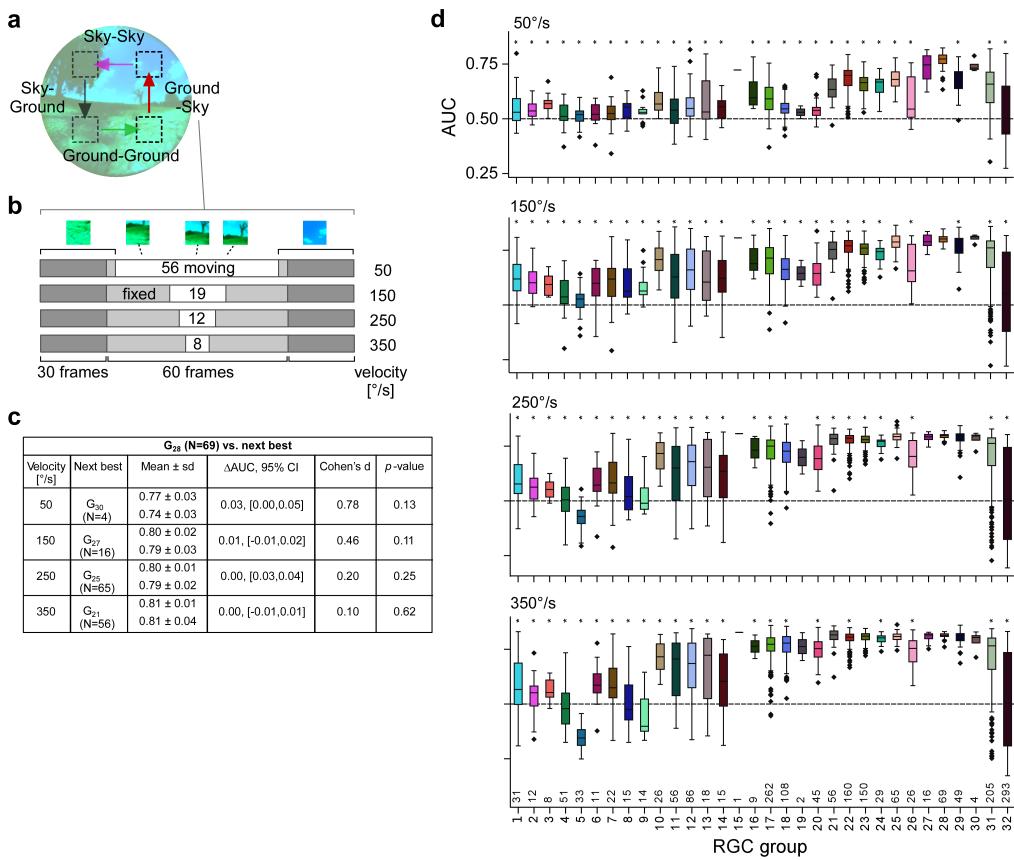


Figure VIII 6-figure supplement 3. (a) Illustration transition stimulus paradigm (from Figure 7h). (b) Structure of stimuli for different velocities, using a ground-to-sky transition as an example. (c) Statistics of the area under the ROC curve (AUC) for the sky-ground detection task in the simulation for different velocities (G₂₈ vs. the next-best RGC group). Columns (from left): mean \pm standard deviation of AUC values (top: G₂₈; bottom: the respective best next RGC type); difference in mean AUC and corresponding bootstrapped 95% confidence intervals; Cohen's d and p-value of a two-sample permutation test with 100,000 repeats. (d) Boxplots of AUC distributions per cell type for the different velocities (plots like in Figure 7g,j).